Appendix A: Search Strategies

Number of citations in ()
/ after an index term indicates that all subheadings were selected.
* before an index term indicates that that term was focused - i.e. limited to records where major MeSH/Emtree term.
"exp" before an index term indicates that the term was exploded.
.tw. indicates a search for a term in title/abstract.
.mp. indicates a free text search for a term.
.pt. indicates a search for a publication type.
$ at the end of a term indicates that this term has been truncated.
? in the middle of a term indicates the use of a wildcard.
adj indicates a search for two terms where they appear adjacent to one another.
sh indicates a search term for subheading.

MEDLINE (OVID) for Randomized Controlled Trials Using the Cochrane Highly Sensitive and Specific Search Strategy (Sensitivity and Precision Maximizing Version 2008)

1. Coronary Artery Disease/ or Coronary Disease/
2. Myocardial Ischemia/
3. Angina Pectoris/ or Angina, Unstable/
4. Angina Pectoris/ or Arterial Occlusive Diseases/
5. Peripheral Vascular Diseases/
6. Vascular Diseases/
7. Atherosclerosis/
8. Cardiovascular Diseases/
9. Carotid Artery Diseases/
10. (((preserved adj left) or (stable adj cad) or (stable adj chd) or (stable adj coronary) or (preserved adj coronary) or (preserved adj systolic) or (preserved adj ventricular) or (preserved adj lvef) or (preserved adj ef) or (preserved adj ejection)) or (intact adj left) or (intact adj systolic) or (intact adj ventricular) or (intact adj lvef) or (intact adj ef) or (normal adj systolic) or (normal adj ventricular) or (normal adj lvef) or (normal adj ef)).mp
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12. randomized controlled trial.pt.
13. controlled clinical trial.pt.
14. randomized.ab.
15. placebo.ab.
16. clinical trials as topic.sh.
17. randomly.ab.
18. trial.ti.
19. 12 or 13 or 14 or 15 or 16 or 17 or 18
20. humans.sh.
21. 19 and 20
22. (alacepril or benazepril or captopril or ceronapril or cilazapril or delapril or enalapril or fosinopril or imidapril or libenzapril or lisinopril or moexipril or moveltipril or pentopril or perindopril or quinapril or ramipril or spirapril or temocapril or teprotide or trandolapril or zofenopril).mp.
23. (losartan or olmesartan or telmisartan or valsartan or eprosartan or candesartan or tasosartan or irbesartan).mp.
24. Angiotensin-Converting Enzyme Inhibitors/
25. Angiotensin II Type 1 Receptor Blockers/
26. (ACEI or ARB).mp.

27. 22 or 23 or 24 or 25 or 26
28. 11 and 21 and 27

Appendix A: Search Strategies

CENTRAL (OVID) for Randomized Controlled Trials

1. (alacepril or benazepril or captopril or ceronapril or cilazapril or delapril or enalapril or fosinopril or imidapril or libenzapril or lisinopril or moexipril).mp.
2. (moveltipril or pentopril or perindopril or quinapril or ramipril or spirapril or temocapril or teprotide or trandolapril or zofenopril).mp.
3. (losartan or olmesartan or telmisartan or valsartan or eprosartan or candesartan or tasosartan or irbesartan).mp.
4. Angiotensin-Converting Enzyme Inhibitors/
5. Angiotensin II Type 1 Receptor Blockers/
6. (ACEI or ARB).mp.
7. 1 or 2 or 3 or 4 or 5 or 6
8. Coronary Artery Disease/ or Coronary Disease/
9. Myocardial Ischemia/
10. Angina Pectoris/ or Angina, Unstable/
11. Arterial Occlusive Diseases/
12. Peripheral Vascular Diseases/
13. Vascular Diseases/
14. Atherosclerosis/
15. Cardiovascular Diseases/
16. Carotid Artery Diseases/
17. (((preserved adj left) or (stable adj cad) or (stable adj chd) or (stable adj coronary) or (preserved adj coronary) or (preserved adj systolic) or (preserved adj ventricular) or (preserved adj lvef) or (preserved adj ef) or (preserved adj ejection)) or (intact adj left) or (intact adj systolic) or (intact adj ventricular) or (intact adj lvef) or (intact adj ef) or (normal adj systolic) or (normal adj ventricular) or (normal adj lvef) or (normal adj ef)).mp
18. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
19. **7 and 18**

EMBASE (Silver Platter) for Randomized Controlled Trials Using the McMaster Health Information Research Unit (HiRU) highly sensitive, highly specific EMBASE search strategy for treatment articles that minimizes differences between sensitivity and specificity

(((preserved adj left) or (stable adj cad) or (stable adj chd) or (stable adj coronary) or (preserved adj coronary) or (preserved adj systolic) or (preserved adj ventricular) or (preserved adj lvef) or (preserved adj ef) or (preserved adj ejection)) or (intact adj left) or (intact adj systolic) or (intact adj ventricular) or (intact adj lvef) or (intact adj ef) or (normal adj systolic) or (normal adj ventricular) or (normal adj lvef) or (normal adj ef)) and (((angiotensin converting enzyme inhibitor or ACE inhibitor or ACEI or arb or angiotensin receptor blocker or angiotensin ii type 1 receptor blocker) or (alacapril or benazepril or captopril or ceronapril or cilazapril or delapril or enalapril or fosinopril or imidapril or libenzapril or lisinopril or moexipril or moveltipril orpentopril or perinodopril or quinapril or ramipril or spirapril or temocapril or teprotide or trandolapril or zofenopril or losartan or olmesartan or telmisartan or valsartan or eprosartan or can desartan or tasosartan or irbesartan)) and (((random) in AB) or (double-blind) or (placebo) or ((random) in TI)))

Appendix A: Search Strategies

MEDLINE (OVID) for Observational Studies using the Scottish Intercollegiate Guidelines Network Observational Study MEDLINE Search Filter (available at: http://www.sign.ac.uk/methodology/filters.html)

1. epidemiologic studies/
2. exp case control studies/
3. exp Cohort Studies/
4. case control.tw.
5. (cohort adj (study or studies)).tw.
6. cohort analy$.tw.
7. (follow up adj (study or studies)).tw.
8. (observational adj (study or studies)).tw.
9. longitudinal.tw.
10. retrospective.tw.
11. cross sectional.tw.
12. Cross-Sectional Studies/
13. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
14. (alacepril or benazepril or captopril orceronapril or cilazapril or delapril or enalapril or fosinopril or imidapril or libenzapril orlisinopril or moexipril).mp.
15. (moveltipril or pentopril or perindopril or quinapril or ramipril or spirapril or temocapril or teprotide or trandolapril or zofenopril).mp.
16. (losartan or olmesartan or telmisartan or valsartan or eprosartan or candesartan or tasosartan or irbesartan).mp.
17. Angiotensin-Converting Enzyme Inhibitors/
18. Angiotensin II Type 1 Receptor Blockers/
19. (ACEI or ARB).mp.
20. 14 or 15 or 16 or 17 or 18 or 19
21. (((preserved adj left) or (stable adj cad) or (stable adj chd) or (stable adj coronary) or 22. (preserved adj coronary) or (preserved adj systolic) or (preserved adj ventricular) or (preserved adj lvef) or (preserved adj ef) or (preserved adj ejection)) or (intact adj left) or (intact adj systolic) or (intact adj ventricular) or (intact adj lvef) or (intact adj ef) or (normal adj systolic) or (normal adj ventricular) or (normal adj lvef) or (normal adj ef)).mp
22. **13 and 20 and 21**

Appendix A: Search Strategies

EMBASE (Silver Platter) for Observational Studies using the Scottish Intercollegiate Guidelines Network Observational Study EMBASE Search Filter (available at: http://www.sign.ac.uk/methodology/filters.html)

1. Clinical study/
2. Case control study
3. Family study/
4. Longitudinal study/
5. Retrospective study/
6. Prospective study/
7. Randomized controlled trials/
8. 6 not 7
9. Cohort analysis/
10. (Cohort adj (study or studies)).mp.
11. (Case control adj (study or studies)).tw.
12. (follow up adj (study or studies)).tw.
13. (observational adj (study or studies)).tw.
14. (epidemiologic$ adj (study or studies)).tw.
15. (cross sectional adj (study or studies)).tw.
16. Or/1-5,8-15
17. (((preserved adj left) or (stable adj cad) or (stable adj chd) or (stable adj coronary) or (preserved adj coronary) or (preserved adj systolic) or (preserved adj ventricular) or (preserved adj lvef) or (preserved adj ef) or (preserved adj ejection)) or (intact adj left) or (intact adj systolic) or (intact adj ventricular) or (intact adj lvef) or (intact adj ef) or (normal adj systolic) or (normal adj ventricular) or (normal adj lvef) or (normal adj ef)).mp
18. **16 AND 17**

Appendix A: Search Strategies

MEDLINE (OVID) for Systematic Reviews Using the Cochrane Highly Sensitive and Specific Search Strategy (Sensitivity and Precision Maximizing Version 2008)

1. (((preserved adj left) or (stable adj cad) or (stable adj chd) or (stable adj coronary) or (preserved adj coronary) or (preserved adj systolic) or (preserved adj ventricular) or (preserved adj lvef) or (preserved adj ef) or (preserved adj ejection)) or (intact adj left) or (intact adj systolic) or (intact adj ventricular) or (intact adj lvef) or (intact adj ef) or (normal adj systolic) or (normal adj ventricular) or (normal adj lvef) or (normal adj ef)).mp
2. (alacepril or benazepril or captopril or ceronapril or cilazapril or delapril or enalapril or fosinopril or imidapril or libenzapril or lisinopril or moexipril).mp.
3. (moveltipril or pentopril or perindopril or quinapril or ramipril or spirapril or temocapril or teprotide or trandolapril or zofenopril).mp.
4. (losartan or olmesartan or telmisartan or valsartan or eprosartan or candesartan or tasosartan or irbesartan).mp.
5. 2 or 3 or 4
6. (angiotensin-converting enzyme inhibitors or angiotensin II type 2 receptor blockers or ACEI or ARB).mp.
7. 5 or 6
8. (coronary artery disease or coronary disease or myocardial ischemia or angina pectoris or unstable angina or aterial occlusive diseases or peripheral vascular disease or vascular disease or atherosclerosis or cardiovascular diseases or carotid artery diseases).mp.
9. 1 or 8
10. 7 or 9
11. meta-analysis.pt.
12. search.tw.
13. cochrane database of systematic reviews.jn.
14. medline or systematic review.tw.
15. 11 or 12 or 13 or 14
16. **10 AND 15**

Appendix A: Search Strategies

Cochrane Database of Systematic Reviews (OVID) for Systematic Reviews

1. (((preserved adj left) or (stable adj cad) or (stable adj chd) or (stable adj coronary) or (preserved adj coronary) or (preserved adj systolic) or (preserved adj ventricular) or (preserved adj lvef) or (preserved adj ef) or (preserved adj ejection)) or (intact adj left) or (intact adj systolic) or (intact adj ventricular) or (intact adj lvef) or (intact adj ef) or (normal adj systolic) or (normal adj ventricular) or (normal adj lvef) or (normal adj ef)).mp
2. (alacepril or benazepril or captopril or ceronapril or cilazapril or delapril or enalapril or fosinopril or imidapril or libenzapril or lisinopril or moexipril).mp.
3. (moveltipril or pentopril or perindopril or quinapril or ramipril or spirapril or temocapril or teprotide or trandolapril or zofenopril).mp.
4. (losartan or olmesartan or telmisartan or valsartan or eprosartan or candesartan or tasosartan or irbesartan).mp.
5. 2 or 3 or 4
6. (angiotensin-converting enzyme inhibitors or angiotensin II type 2 receptor blockers or ACEI or ARB).mp.
7. 5 or 6
8. (coronary artery disease or coronary disease or myocardial ischemia or angina pectoris or unstable angina or aterial occlusive diseases or peripheral vascular disease or vascular disease or atherosclerosis or cardiovascular diseases or carotid artery diseases).mp.
9. 1 or 8
10. **7 AND 9**

Appendix B: List of Excluded Studies

Efficacy/Harms Search

1. Ahmad J, Siddiqui MA, Ahmad H. Effective postponement of diabetic nephropathy with enalapril in normotensive type 2 diabetic patients with microalbuminuria. Diabetes Care 1997;20(10):1576-58.
2. Aksnes TA, Kjeldsen SE, Rostup M, et al. Impact of new-onset diabetes mellitus on cardiac outcomes in the Valsartan Antihypertensive Long-term Use Evaluation (VALUE) trial population. Hypertension 2007;50(3):467-73.
3. Alderman EL, Botas J. Selection of revascularization for patients with stable angina pectoris. Coron Artery Dis 1993;4(12):1061-7.
4. Al-Khadra AS, Salem DN, Rand WM, et al. Antiplatelet agents and survival: a cohort analysis from the Studies of Left Ventricular Dysfunction (SOLVD) trial. J Am Coll Cardiol 1998;31(2):419-25.
5. Al-Khadra AS, Salem DN, Rand WM, et al. Antiplatelet agents and survival: a cohort analysis from the Studies of Left Ventricular Dysfunction (SOLVD) trial. J Am Coll Cardiol 1998;31(2):419-25.
6. ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). JAMA 2002;288(23):2981-97.
7. Ambrosioni E, Borghi C, Magnani B. Early treatment of acute myocardial infarction with angiotensin-converting enzyme inhibition: safety considerations. SMILE pilot study working party. Am J Cardiol 1991;68(14):101D-110D.
8. Anavekar NS, McMurray JJ, Velazquez EJ, et al. Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction. N Engl J Med 2004;351(13):1285-95.
9. Anavekar NS, Solomon SD, McMurray JD, et al. Comparison of renal function and cardiovascular risk following acute myocardial infarction in patients with and without diabetes mellitus. Am J Cardiol 2008;101(7):925-9.
10. Anderson C. Rationale and design of the cardiac magnetic resonance imaging substudy of The ONTARGET Trial Programme. J Int Med Res 2005;33(Suppl 1):50A-57A.
11. Anderson TJ, Elstein E, Haber H, et al. Comparative study of ACE-inhibition, angiotensin II antagonism, and calcium channel blockade on flow-mediated vasodilation in patients with coronary disease (BANFF study). J Am Coll Cardiol 2000;35(1):60-6.
12. Arima H, Hart RG, Colman S, et al. Perindopril-based blood pressure-lowering reduces major vascular events in patients with atrial fibrillation and prior stroke or transient ischemic attack. Stroke 2005;36(10):2164-9.
13. Arima H, Tzourio C, Butcher K, et al. Prior events predict cerebrovascular and coronary outcomes in the PROGRESS trial. Stroke 2006;37(6):1497-1502.
14. Arnett DK, Davis BR, Ford CE, et al. Pharmacogenetic association of the angiotensin-converting enzyme insertion/deletion polymorphism on blood pressure and cardiovascular risk in relation to antihypertensive treatment: the Genetics of Hypertension-Associated Treatment (GenHAT) study. Circulation 2005;111(25):3374-83.

Appendix B: List of Excluded Studies

15. Asselbergs FW, Diercks GF, Hillege HL, et al. Effects of fosinopril and pravastatin on cardiovascular events in subjects with microalbuminuria. Circulation 2004;110(18):2809-16.
16. Asselbergs FW, Hillege HL, van Gilst WH. Framingham score and microalbuminuria: combined future targets for primary prevention? Kidney Int 2004;6(Suppl 92):S111-4.
17. Athyros VG, Mikhailidis DP, Papageorgiou AA, et al. Effect of statins and ACE inhibitors alone and in combination on clinical outcome in patients with coronary heart disease. J Hum Hypertens 2004;18(11):781-8.
18. Atthobari J, Asselbergs FW, Boersma C, et al. Cost-effectiveness of screening for albuminuria with subsequent fosinopril treatment to prevent cardiovascular events: A pharmacoeconomic analysis linked to the prevention of renal and vascular endstage disease (PREVEND) study and the prevention of renal and vascular endstage disease intervention trial (PREVEND IT). Clin Ther 2006;28(3):432-44.
19. Atthobari J, Brantsma AH, Gansevoort RT, et al. The effect of statins on urinary albumin excretion and glomerular filtration rate: results from both a randomized clinical trial and an observational cohort study. Nephrol Dial Transplant 2006;21:3106-14.
20. Baba S, and the J-MIND Study Group. Nifedipine and enalapril equally reduce the progression of nephropathy in hypertensive type 2 diabetics. Diabetes Res Clin Pract 2001;54(3):191-201.
21. Bakins GL. Benefits of combination therapy for achieving goal blood pressure in high CV risk patients. Cardiovasc J S Afr 2001;12:54-5.
22. Bakris GL, Ruilope L, Locatelli F, et al. Treatment of microalbuminuria in hypertensive subjects with elevated cardiovascular risk: results of the IMPROVE trial. Kidney Int 2007;72:879-85.
23. Barzilay JI, Jones CL, Davis BR. Baseline characteristics of the diabetic participants in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). Diabetes Care 2001;24(4):654-8.
24. Baumgart P. [Antihypertensive therapy: risk stratification in diabetes and cardiac diseases.] MMW Fortschr Med 2006;148(11):57-60. (German).
25. Bayliss J, Canepa-Anson R, Norell M, et al. The renal response to neuroendocrine inhibition in chronic heart failure: double-blind comparison of captopril and prazosin. Eur Heart J 1986;7(10):877-84.
26. Berger PB, Holmes DR, Ohman EM, et al. Restenosis, reocclusion and adverse cardiovascular events after successful balloon angioplasty of occluded versus nonoccluded coronary arteries. Results from the Multicenter American Research Trial With Cilazapril After Angioplasty to Prevent Transluminal Coronary Obstruction and Restenosis (MARCATOR). J Am Coll Cardiol 1996;27(1):1-7.
27. Berl T, Hunsicker LG, Lewis JB, et al. Cardiovascular outcomes in the irbesartan diabetic nephropathy trial of patients with type 2 diabetes and overt nephropathy. Ann Intern Med 2003;138(7):542-9.
28. Berl T, Hunsicker LG, Lewis JB, et al. Impact of achieved blood pressure on cardiovascular outcomes in the Irbesartan Diabetic Nephropathy Trial. J Am Soc Nephrol 2005;16(7):2170-9.
29. Biasucci LM, Lombardi M, Piro M, et al. Irbesartan significantly reduces C reactive protein concentrations after 1 month of treatment in unstable angina. Heart 2005;91(5):670-1

Appendix B: List of Excluded Studies

30. Bibbins-Domingo K, Lin F, Vittinghoff E, et al. Renal insufficiency as an independent predictor of mortality among women with heart failure. J Am Coll Cardiol 2004;44(8):1593-1600.
31. Bjorholt I, Andersson FL, Kahan T, et al. The cost-effectiveness of ramipril in the treatment of patients at high risk of cardiovascular events: a Swedish sub-study to the HOPE study. J Intern Med 2002;251(6):508-17.
32. Black HR, Davis B, Barzilay J, et al. Metabolic and clinical outcomes in nondiabetic individuals with the metabolic syndrome assigned to chlorthalidone, amlodipine, or lisinopril as initial treatment for hypertension: a report from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). Diabetes Care 2008;31(2):353-60.
33. Blankenberg S, McQueen MJ, Smieja M, et al. Comparative impact of multiple biomarkers and N-Terminal pro-brain natriuretic peptide in the context of conventional risk factors for the prediction of recurrent cardiovascular events in the Heart Outcomes Prevention Evaluation (HOPE) Study. Circulation 2005;114(3):201-8.
34. Boersma C, Carides GW, Atthobari J, et al. An economic assessment of losartan-based versus atenolol-based therapy in patients with hypertension and left-ventricular hypertrophy: results from the Losartan Intervention For Endpoint reduction (LIFE) study adapted to The Netherlands. Clin Ther 2007;29(5):963-71.
35. Bohm M, Baumhakel M, Probstfield JL, et al. Sexual function, satisfaction, and association of erectile dysfunction with cardiovascular disease and risk factors in cardiovascular high-risk patients: substudy of the ONgoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial/Telmisartan Randomized AssessmeNT Study in ACE-INtolerant Subjects with Cardiovascular Disease (ONTARGET/TRANSCEND). Am Heart J 2007;154(1):94-101.
36. Boldt J, Rothe G, Schindler E, et al. Can clonidine, enoximone, and enalaprilat help to protect the myocardium against ischaemia in cardiac surgery? Heart 1996;76(3):207-13.
37. Boner G, Cooper ME, McCarroll K, et al. Adverse effects of left ventricular hypertrophy in the reduction of endpoints in NIDDM with the angiotensin II antagonist losartan (RENAAL) study. Diabetologia 2005;48(10):1980-7.
38. Bots ML, Remme WJ, Luscher TF, et al. ACE inhibition and endothelial function: main findings of PERFECT, a sub-study of the EUROPA trial. Cardiovasc Drugs Ther 2007;21(4):269-79.
39. Bots ML, Remme WJ, Luscher TF, et al. PERindopril-Function of the Endothelium in Coronary Artery Disease Trial: The PERFECT Study-Sub Study of EUROPA: Rationale and Design. Cardiovasc Drugs Ther 2002;16(3):227-36.
40. Boulanger JM, Hill MD. Morbidity and mortality after stroke--eprosartan compared with nitrendipine for secondary prevention: principal results of a prospective randomized controlled study (MOSES). Stroke 2006;37(2):335-6.
41. Brener SJ, Ivanc TB, Poliszczuk R, et al. Antihypertensive therapy and regression of coronary artery disease: insights from the Comparison of Amlodipine versus Enalapril to Limit Occurrences of Thrombosis (CAMELOT) and Norvasc for Regression of Manifest Atherosclerotic Lesions by Intravascular Sonographic Evaluation (NORMALISE) trials. Am Heart J 2006;152(6):1059-63.

Appendix B: List of Excluded Studies

42. Brenner BM, Cooper ME, Zeeuw DD, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med 2001;345(12):861-9.
43. Briggs A, Mihaylova B, Sculpher M, et al. Cost effectiveness of perindopril in reducing cardiovascular events in patients with stable coronary artery disease using data from the EUROPA study. Heart 2007;93(9):1081-6.
44. Burduli FY, Khadzhidis PK, Vatsadze TG, et al. [Use of prazosin and capoten in the treatment of heart failure in patients with ischemic heart disease.] Kardiologia 1989;29:49-52. (Russian).
45. Campbell DJ , Woodward M, Chalmers JP, et al. Perindopril-based blood pressure-lowering therapy reduces amino-terminal-pro-B-type natriuretic peptide in individuals with cerebrovascular disease. J Hypertens 2007;25(3):699-705.
46. Capri S, Perlini S. Cost-effectiveness in Italy of preventive treatment with ramipril in patients at high risk of cardiovascular events. Curr Med Res Opin 2005;21(6):913-21.
47. Carson P, Massie BM, Mckelvie R, et al. The Irbesartan in Heart Failure with Preserved Systolic Function. J Card Fail 2005;11(8):576-85.
48. Cashin-Hemphill L, Holmvang G, Chan RC, et al. Angiotensin-converting enzyme inhibition as antiatherosclerotic therapy: no answer yet. QUIET Investigators. QUinapril Ischemic Event Trial. Am J Cardiol 1999;83(1):43-7.
49. Cashin-Hemphill L, Holmvang G, Chan RC, et al. Angiotensin-converting enzyme inhibition as antiatherosclerotic therapy: no answer yet. QUIET Investigators. QUinapril Ischemic Event Trial. Am J Cardiol 1999;83(1):43-7.
50. Catalano M, Libretti A. Captopril for the treatment of patients with hypertension and peripheral vascular disease. Angiology 1985;36(5):293-6.
51. Ceconi C, Fox KM, Remme W, et al. ACE inhibition with perindopril and endothelial function. Results of a substudy of the EUROPA study: PERTINENT. Cardiovasc Res 2007;73(1):237-46.
52. Cesari M, Kritchevsky SB, Atkinson HH, et al. Angiotensin-converting enzyme inhibition and novel cardiovascular risk biomarkers: results from the Trial of Angiotensin Converting Enzyme Inhibition and Novel cardiovascular risk factors (TRAIN) study. Am Heart J 2009;157(2):e1-e8.
53. Chaitman BR, Ivleva AY, Ujda M, et al. Antianginal efficacy of omapatrilat in patients with chronic angina pectoris. Am J Cardiol 2005;95(11):1283-9.
54. Charbonneau F. Background rationale for a study to assess normalization of brachial artery forearm flow function. Can J Cardiol 1998;14(Suppl D):16D-17D.
55. Coca A, Messerli FH, Benetos A, et al. Predicting stroke risk in hypertensive patients with coronary artery disease: a report from the INVEST trial. Stroke 2008;39(2):343-8.
56. Cohen-Solal A, McMurray JJ, Swedberg K, et al. for the CHARM Investigators. Benefits and safety of candesartan treatment in heart failure are independent of age: insights from the Candesartan in Heart Failure – Assessment of Reduction in Mortality and morbidity programme. Eur Heart J 2008;29(24):3022-8.
57. Colombo GL, Caruggi M, Ottolini C, et al. Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity (CHARM) and resource utilization and costs in Italy. Vasc Health Risk Manag 2008;4(1):223-34.
58. Cooper DeHoff RM, Handberg EM, Cohen J, et al. Characteristics of contemporary patients with hypertension and coronary artery disease. Clin Cardiol 2004;27(10):571-6.

Appendix B: List of Excluded Studies

59. Dagenais GR, Yi Q, Lonn E, et al. Impact of cigarette smoking in high-risk patients participating in a clinical trial. A substudy from the Heart Outcomes Prevention Evaluation (HOPE) trial. Eur J Cardiovasc Prev Rehabil 2005;12(1):75-81.
60. Dahlof B, Devereux RB, Kjeldsen SE, et al. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. Lancet 2002;359:995-1003.
61. Daly CA, Hildebrandt P, Bertrand M, et al. Adverse prognosis associated with the metabolic syndrome in established coronary artery disease: data from the EUROPA trial. Heart 2007;93(11):1406-11.
62. Dauterman KW, Go AS, Rowell R, et al. Congestive heart failure with preserved systolic function in a statewide sample of community hospitals. J Card Fail 2001;7(3):221-8.
63. Dauterman KW, Go AS, Rowell R, et al. Congestive heart failure with preserved systolic function in a statewide sample of community hospitals. J Card Fail 2001;7(3):221-8.
64. Davis BR, Arnett DK, Boerwinkle E, et al. Antihypertensive therapy, the alpha-adducin polymorphism, and cardiovascular disease in high-risk hypertensive persons: the Genetics of Hypertension-Associated Treatment Study. The Pharmacogenomics Journal 2007;7(2):112-22.
65. Davis BR, Cutler JA, Gordon D, et al. Rationale and design for the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). ALLHAT Research Group. Am J Hypertens 1996;9(4 pt 1):342-60.
66. Davis BR, Kostis JB, Simpson LM, et al. for the ALLHAT Collaborative Research Group. Heart failure with preserved and reduced left ventricular ejection fraction in the antihypertensive and lipid-lowering treatment to prevent heart attack trial. Circulation 2008;118(22):2259-67.
67. de Simone G, Wachtell K, Palmieri V, et al. Body build and risk of cardiovascular events in hypertension and left ventricular hypertrophy: the LIFE (Losartan Intervention For Endpoint reduction in hypertension) study. Circulation 2005;111(15):1924-31.
68. de Zeeuw D, Remuzzi G, Parving HH, et al. Albuminuria, a therapeutic target for cardiovascular protection in type 2 diabetic patients with nephropathy. Circulation 2004;110(8):921-7.
69. Desmet W, Vrolix M, Scheerder ID, et al. Angiotensin-converting enzyme inhibition with fosinopril sodium in the prevention of restenosis after coronary angioplasty. Circulation 1994;89:385-92.
70. Devereux RB, Dahlof B, Kjeldsen SE, et al. Effects of losartan or atenolol in hypertensive patients without clinically evident vascular disease: a substudy of the LIFE randomized trial. Ann Intern Med 2003;139(3):169-77.
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Appendix C: Additional Evidence Tables and Analyses

Abbreviations

Acronym/Abbreviation	Definition
ACE	Angiotensin Converting Enzyme
ACEI	Angiotensin Converting Enzyme Inhibitor
ADE	Adverse Drug Event
AHR	Adjusted Hazard Ratio
AMSTAR	Assess the Methodological quality of SysteMAtic Review
APRES	Angiotensin-converting Enzyme inhibition Post Revascularization Study
ARB	Angiotensin Receptor Blocker
CABG	Coronary Artery Bypass Grafting
CAD	Coronary Artery Disease
CAMELOT	Comparison of Amlodipine vs Enalapril to Limit Occurrences of Thrombosis
CCB	Calcium Channel Blocker
CHF	Congestive Heart Failure
CI	Confidence Interval
CV	Cardiovascular
DM	Diabetes Mellitus
EKG	Electrocardiogram
EUROPA	EURopean trial On reduction of cardiac events with Perindopril in stable coronary Artery disease
FOSIDIAL	FOSInopril in DIALysis
F/U	Follow-Up
GRADE	Grading of Recommendations Assessment, DEvelopment
HF	Heart Failure
HOPE	Heart Outcomes Prevention Evaluation
HR	Hazard Ratio
HTN	Hypertension
IC	Intermittent Claudication
IHD	Ischemic Heart Disease
IMAGINE	Ischemia Management with Accupril post-bypass Graft via Inhibition of the coNverting Enzyme
JMIC-B	Japan Multicenter Investigation for Cardiovascular Diseases-B
LVEF	Left Ventricular Ejection Fraction
LVH	Left Ventricular Hypertrophy
MARCATOR	Multicenter American Research trial with Cilazapril After angioplasty to prevent Transluminal coronary Obstruction and Restenosis
MI	Myocardial Infarction
N/A	Not Applicable
NR	Not Reported
ONTARGET	ONgoing Telmisartan Alone in combination with Ramipril Global Endpoint Trial
OR	Odds Ratio
PARIS	Effect of ACE inhibitors on angiographic restenosis after coronary stenting
PART-2	Prevention of Atherosclerosis with Ramipril Trial-2
PCI	Percutaneous Coronary Intervention

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PEACE	Prevention of Events with Angiotensin Converting Enzyme Inhibition
PTCA	Percutaneous Transluminal Coronary Angioplasy
PVD	Peripheral Vascular Disease
QUIET	Quinapril Ischemic Event Trial
RCT	Randomized Controlled Trial
RR	Relative Risk
SB	Single Blind
SCAT	Simvastatin/enalapril Coronary Atherosclerosis Trial
SMILE-ISCHEMIA	Survival of Myocardial Infarcton Long-term Evaluation-ISCHEMIA
SMT	Standard Medical Therapy
TIA	Transient Ischemic Attack
TRANSCEND	Telmisartan Ransomized AssessmeNt Study in ACE iNtolerant subjects with cardiovascular Disease
SCR	Scientific Resource Center

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Appendix Table 1. Pertinent Systematic Reviews

Reference	Inclusion Criteria	Total Studies Included	Total Pts Included	AMSTAR rating
Al-Mallah 2006[92]	All randomized, placebo controlled trials of ACEIs use in patients with CAD and preserved LV function (LVEF≥40%)	6	33,500	7/11
Dagenais 2006[93]	HOPE, EUROPA and PEACE (the three main large trials of ACEIs in patients with atherosclerosis, but without heart failure or LSVD)	3	29,805	2/11
Danchin 2006[94]	All placebo-controlled randomized trials with a follow-up of 2 years or longer performed in patients who had stable CAD and either no signs or symptoms of heart failure or no documented LV dysfunction (no LVEF<35%)	7	33,960	9/11
Saha 2007[95]	All randomized, placebo controlled clinical trials with mean study duration of at least 12 months, a use of a tissue-selective ACEI (ramipril, perindopril, quinapril, or trandolapril), and strict inclusion of patients with cardiovascular disease who either had documented EKG evidence of normal left ventricular function (LVEF>40%) or had no clinical symptoms of CHF at the time of randomization	4	31,555	7/11
Lang 2008[96]	All randomized, placebo controlled clinical trials with mean study duration of at least 12 months, a use of a tissue-selective ACEI (ramipril, perindopril, quinapril, or trandolapril), patients with documented DM with evidence of normal left ventricular systolic function or who had no symptoms of congestive heart failure at the onset of the study, and risk factors in addition to DM, according to the Framingham classification	4	10,328	6/11
Saha 2008[97]	All RCTs with mean follow-up period of at least 12 months, and that compared effects of tissue-selective ACEI (ramipril, perindopril, quinapril, or trandolapril), with placebo, in patients with known DM who either had documented evidence of normal left ventricular systolic function or had no clinical symptoms of congestive heart failure at the start of the study	4	10,328	6/11

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Appendix Table 2. KQ1 Total Mortality - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 CV Risk Factor	Death from any cause	Ramipril Placebo	482/4645 569/4652	RR 0.84 (0.75 to 0.95)
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	All clinical events resulting in death	Ramipril Placebo	16/308 25/309	RR 0.64 (0.34 to 1.20)
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	Death	Enalapril Placebo	8/229 11/231	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	Total mortality	Perindopril Placebo	375/6110 420/6108	1-RR 11% (-2% to 23%)
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	Cardiovascular + non-cardiovascular deaths	Candesartan Control	4/194 11/203	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	All-cause mortality	Enalapril Amlodipine Placebo	8/673 7/663 6/655	HR 1.26 (0.44 to 3.65)† HR 0.92 (0.33 to 2.53)¶ HR 1.14 (0.38 to 3.40)‡
JMIC-B, 2004[46]	RCT	Hypertension and CAD	Total mortality	ACEI∝ Nifedipine	15/822 12/828	RR 0.76 (0.35 to 1.63)∂
PEACE, 2004[47]	RCT	Documented CAD	Death from any cause	Trandolapril Placebo	299/4158 334/4132	HR 0.89 (0.76 to 1.04)
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	All cause death	Fosinopril Placebo	53/196 50/201	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	Mortality	Candesartan Control	0/43 7/37	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	Total mortality	Telmisartan Placebo	364/2954 349/2972	AHR 1.05 (0.91 to 1.22)

† = Enalapril vs placebo; ¶ = Amlodipine vs enalapril; ‡ = Amlodipine vs placebo; ∝ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril; * = Clinical outcome data provided by FOSIDIAL corresponding author; ∂ = Nifidepine vs ACEI

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Appendix Table 3. KQ1 Cardiovascular Mortality - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 CV Risk Factor	Death from cardiovascular causes	Ramipril Placebo	282/4645 377/4652	RR 0.74 (0.64 to 0.87)
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	Death from cardiovascular disease	Ramipril Placebo	8/308 18/309	RR 0.45 (0.19 to 1.03)
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	Cardiac death	Enalapril Placebo	4/229 7/231	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	Cardiovascular mortality	Perindopril Placebo	215/6110 249/6108	1-RR 14% (-3 to 28)
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	Cardiovascular death	Candesartan Control	2/194 9/203	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Cardiovascular death	Enalapril Amlodipine Placebo	5/673 5/663 2/655	HR 2.33 (0.45 to 12.1)† HR 1.07 (0.31 to 3.70)¶ HR 2.46 (0.48 to 12.7)‡
JMIC-B, 2004[46]	RCT	Hypertension and CAD	Cardiac death or sudden death	ACEI∝ Nifedipine	6/822 6/828	RR 0.96 (0.31 to 3.04)∂
PEACE, 2004[47]	RCT	Documented CAD	Death from cardiovascular causes	Trandolapril Placebo	146/4158 152/4132	HR 0.95 (0.76 to 1.19)
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	Cardiovascular death	Fosinopril Placebo	32/196 31/201	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	Cardiovascular death	Telmisartan Placebo	227/2954 223/2972	AHR 1.03 (0.85 to 1.24)

† = Enalapril vs placebo; ¶ = Amlodipine vs enalapril; ‡ = Amlodipine vs placebo; ∝ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril; * = Clinical outcome data provided by FOSIDIAL corresponding author; ∂ = Nifedipine vs ACEI

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Appendix Table 4. KQ1 Nonfatal Myocardial Infarction - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 CV Risk Factor	Acute MI not resulting in death	Ramipril Placebo	260/4645 333/4652	1-RR 23% (9 to 34)
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	Nonfatal MI requiring hospital admission	Ramipril Placebo	18/308 19/309	RR 0.94 (0.49 to 1.80)
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	Nonfatal MI	Enalapril Placebo	7/229 12/231	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) w/o HF	Nonfatal MI (see total MI for definition)	Perindopril Placebo	295/6110 378/6108	1-RR 22% (10 to 33)
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	Nonfatal MI	Candesartan Control	2/194 1/203	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Nonfatal MI	Enalapril Amlodipine Placebo	11/673 14/663 19/655	HR 0.55 (0.26 to 1.15)† HR 1.32 (0.60 to 2.90)¶ HR 0.73 (0.37 to 1.46)‡
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI∝ Nifedipine	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	Nonfatal MI	Trandolapril Placebo	222/4158 220/4132	HR 1.00 (0.83 to 1.20)
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	Nonfatal MI	Fosinopril Placebo	9/196 7/201	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, CV disease, PVD, or DM + end-organ damage	NR	Telmisartan Placebo	NR	NR

† = Enalapril vs placebo; ‡ = Amlodipine vs placebo; ¶ = Amlodipine vs enalapril; ∝ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril; * = Clinical outcome data provided by FOSIDIAL corresponding author

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Appendix Table 5. KQ1 Stroke - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 Risk Factor	Stroke	Ramipril Placebo	156/4645 226/4652	RR 0.68 (0.56 to 0.84)
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	Nonfatal stroke requiring hospital admission	Ramipril Placebo	7/308 4/309	RR 1.67 (0.48 to 5.75)
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, ↑ cholesterol	Stroke	Enalapril Placebo	2/229 9/231	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) w/o HF	Stroke	Perindopril Placebo	98/6110 102/6108	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Stroke or TIA	Enalapril Amlodipine Placebo	8/673 6/663 12/655	HR 0.66 (0.27 to 1.62)† HR 0.76 (0.26 to 2.20)¶ HR 0.50 (0.19 to 1.32)‡
JMIC-B, 2004[46]	RCT	HTN and CAD	Cerebrovascular accidents	ACEI∝ Nifedipine	16/822 16/828	RR 0.76 (0.56 to 2.02)∂
PEACE, 2004[47]	RCT	Documented CAD	Stroke	Trandolapril Placebo	71/4158 92/4132	HR 0.76 (0.56 to 1.04)
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	Stroke	Fosinopril Placebo	18/196 11/201	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	New focal neurological deficits of vascular origin with s/sx>24h, or death if occurred earlier	Telmisartan Placebo	112/2954 136/2972	AHR 0.83 (0.64 to 1.06)

† = Enalapril vs placebo; ¶ = Amlodipine vs enalapril; ‡ = Amlodipine vs placebo; ∝ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril; * = Clinical outcome data provided by FOSIDIAL corresponding author; ∂ = Nifedipine vs ACEI

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Appendix Table 6. KQ1 Composite – Cardiovascular Mortality, Nonfatal Myocardial Infarction, or Stroke – Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 Risk Factor	Ramipril Placebo	651/4645 826/4652	RR 0.78 (0.70 to 0.86)
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	Ramipril Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	Enalapril Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) w/o HF	Perindopril Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	Candesartan Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Enalapril Amlodipine Placebo	NR	NR
JMIC-B, 2004[46]	RCT	HTN and CAD	ACEI$^{\propto}$ Nifedipine	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	Trandolapril Placebo	396/4158 420/4132	HR 0.93 (0.81 to 1.07)
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	Fosinopril Placebo	48/196 41/201	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	Candesartan Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	Zofenopril Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	Telmisartan Placebo	384/2954 440/2972	AHR 0.86 (0.74 to 1.00)

† = Enalapril vs placebo; ‡ = Amlodipine vs placebo; ¶ = Amlodipine vs enalapril

$\propto$ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril

* = Clinical outcome data provided by FOSIDIAL corresponding author

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 7. KQ1 Atrial Fibrillation - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[40]	RCT	CAD, Stroke, PVD or DM + 1 Risk Factor	Atrial Fibrillation	Ramipril Placebo	86/4291 91/4044	OR 0.92 (0.68 to 1.24)
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	NR	Ramipril Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	NR	Enalapril Amlodipine Placebo	NR	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI$^{\propto}$ Nifedipine	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	NR	Trandolapril Placebo	NR	NR
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	NR	Fosinopril Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	New atrial fibrillation	Telmisartan Placebo	182/2954 180/2972	AHR 1.02 (0.83 to 1.26)

$\propto$ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 8. KQ1 Hospitalizations - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 Risk Factor	NR	Ramipril Placebo	NR	NR
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	Admitted to the hospital at least once	Ramipril Placebo	279/308 289/309	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	NR	Enalapril Amlodipine Placebo	NR	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI$^{\propto}$ Nifedipine	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	NR	Trandolapril Placebo	NR	NR
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	NR	Fosinopril Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	Number of patients hospitalized	Telmisartan Placebo	1477/2954 1526/2972	RR 0.97 (0.93 to 1.02)

$\propto$ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 9. KQ1 Hospitalization For Angina - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 Risk Factor	Hospitalization for unstable angina	Ramipril Placebo	554/4645 565/4652	RR 0.98 (0.87 to 1.10)
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	Unstable angina requiring hospitalization	Ramipril Placebo	45/308 42/309	RR 1.08 (0.71 to 1.65)
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	Hospitalization for angina	Enalapril Placebo	40/229 29/231	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	Hospitalization for worsening angina	Candesartan Control	9/194 14/203	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Hospitalization for angina	Enalapril Amlodipine Placebo	86/673 51/663 84/655	HR 0.98 (0.72 to 1.32)† HR 0.59 (0.42 to 0.84)¶ HR 0.58 (0.41 to 0.82)‡
JMIC-B, 2004[46]	RCT	Hypertension and CAD	Angina pectoris requiring hospitalization	ACEI∝ Nifedipine	56/822 50/828	RR 0.80 (0.55 to 1.18)∂
PEACE, 2004[47]	RCT	Documented CAD	NR	Trandolapril Placebo	NR	NR
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	NR	Fosinopril Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	Angina with hospitalization and ECG changes	Telmisartan Placebo	253/2954 287/2972	HR 0.88 (0.74 to 1.04)

† = Enalapril vs placebo ‡ = Amlodipine vs placebo; ¶ = Amlodipine vs enalapril; ∝ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril; ∂ = Nifedipine vs ACEI

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 10. KQ1 Hospitalization For Heart Failure - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 Risk Factor	Hospitalization for heart failure	Ramipril Placebo	141/4645 160/4652	RR 0.88 (0.70 to 1.10)
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	CHF requiring hospitalization	Ramipril Placebo	7/308 9/309	RR 0.78 (0.29 to 2.09)
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	HF requiring hospital admission	Perindopril Placebo	63/6110 103/6108	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	Hospitalization for HF	Candesartan Control	0/194 2/203	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Hospitalization for CHF	Enalapril Amlodipine Placebo	4/673 3/663 5/655	HR 0.78 (0.21 to 2.90)† HR 0.78 (0.17 to 3.47)¶ HR 0.59 (0.14 to 2.47)‡
JMIC-B, 2004[46]	RCT	Hypertension and CAD	HF requiring hospitalization	ACEI∝ Nifedipine	9/822 12/828	RR 1.25 (0.52 to 2.98)∂
PEACE, 2004[47]	RCT	Documented CAD	CHF as primary cause of hospitalization	Trandolapril Placebo	105/4158 134/4132	HR 0.77 (0.60 to 1.00)
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	NR	Fosinopril Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	Hospitalization for HF or attendance in an acute care setting	Telmisartan Placebo	134/2954 129/2972	HR 1.05 (0.82 to 1.34)

† = Enalapril vs placebo; ‡ = Amlodipine vs placebo; ¶ = Amlodipine vs enalapril; ∝ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril; ∂ = Nifedipine vs ACEI

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 11. KQ1 Revascularization - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 Risk Factor	All CV revasc (CABG, PCI, carotid endarterectomy, peripheral vascular surgery)	Ramipril Placebo	742/4645 852/4652	RR 0.85 (0.77 to 0.94)
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	NR	Ramipril Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	Any revascularization	Enalapril Placebo	16/229 25/231	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	Revasc (CABG or PTCA)	Perindopril Placebo	577/6110 601/6108	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	Revascularization	Candesartan Control	8/194 15/203	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Coronary revascularization	Enalapril Amlodipine Placebo	95/673 78/663 103/655	HR 0.86 (0.65 to 1.14)† HR 0.84 (0.62 to 1.13)¶ HR 0.73 (0.54 to 0.98)‡
JMIC-B, 2004[46]	RCT	Hypertension and CAD	Performance of coronary interventions (PTCA, CABG or stenting)	ACEI∝ Nifedipine	75/822 81/828	RR 1.04 (0.76 to 1.43)∂
PEACE, 2004[47]	RCT	Documented CAD	CABG	Trandolapril Placebo	271/4158 294/4132	HR 0.91 (0.77 to 1.07)
			PCI	Trandolapril Placebo	515/4158 497/4132	HR 1.03 (0.97 to 1.16)
FOSIDIAL, 2006*[48]	RCT	Hemodialysis and LVH	NR	Fosinopril Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan Control	NR	NR

Appendix C: Additional Evidence Tables and Analyses

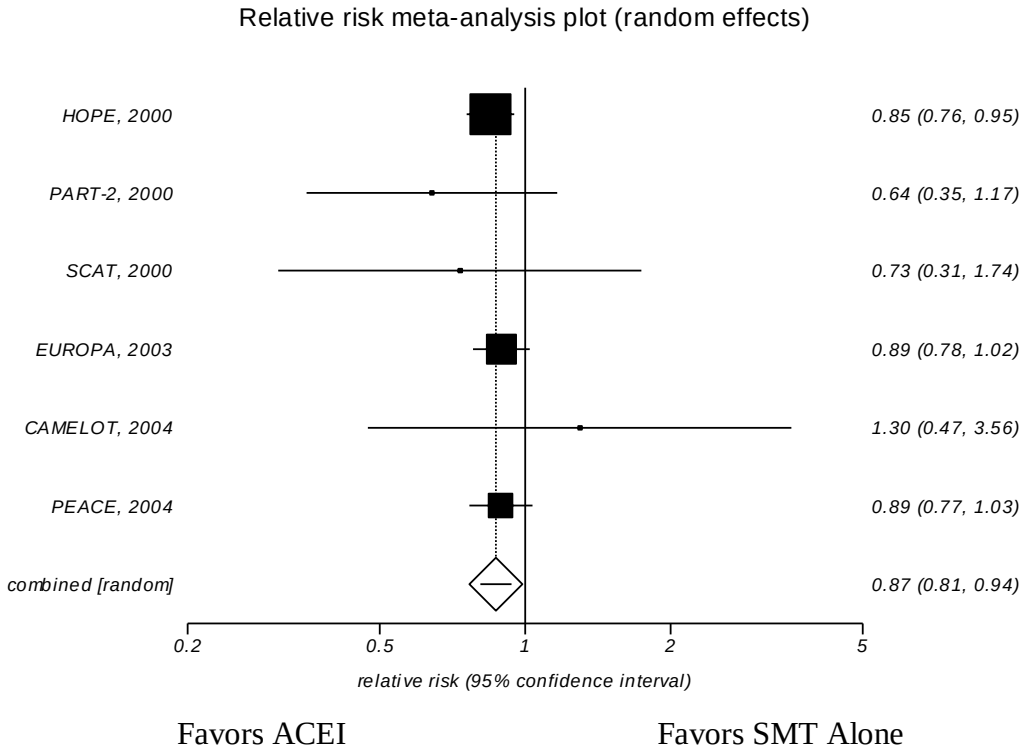
Appendix Table 11 Continued. KQ1 Revascularization - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	Revascularization procedures	Telmisartan Placebo	349/2954 390/2972	HR 0.90 (0.77 to 1.03)

† = Enalapril vs placebo; ‡ = Amlodipine vs placebo; ¶ = Amlodipine vs enalapril; ∝ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril; * = Clinical outcome data provided by FOSIDIAL corresponding author; ∂ = Nifedipine vs ACEI

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 1. KQ1 Total Mortality ACEI Subgroup Analysis - Meta-analysis of randomized placebo-controlled controlled trials in patients with stable ischemic heart disease

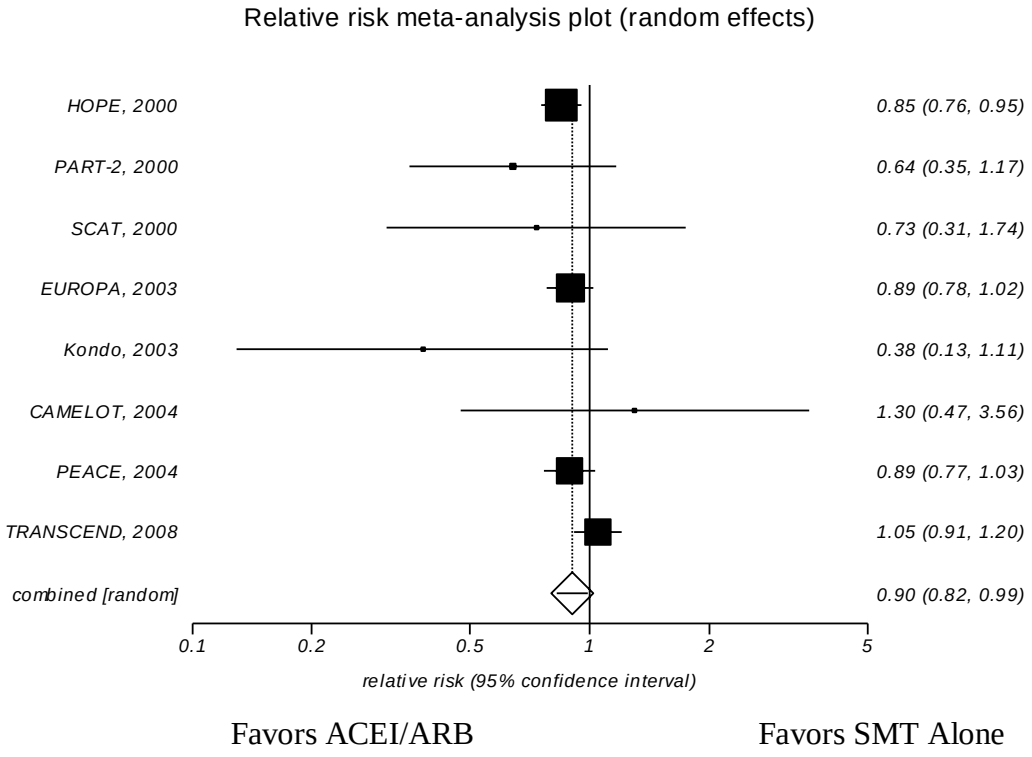


Test for heterogeneity: Cochran Q=2.064483 (df=5) p=0.8402
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 2. KQ1 Total Mortality Sensitivity Analysis - Meta-analysis of randomized placebo-controlled & open-label trials in patients with stable ischemic heart disease

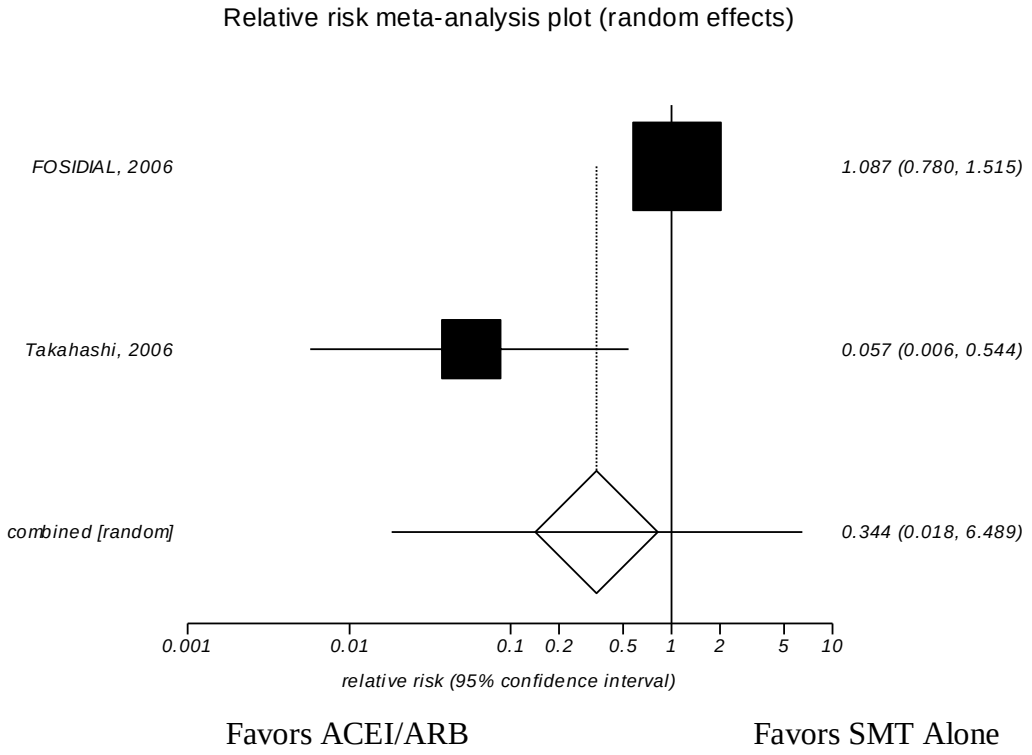


Test for heterogeneity: Cochran Q=9.913118 (df=7) p=0.1936
I^2 statistic=29.4%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 3. KQ1 Total Mortality Sensitivity Analysis - Meta-analysis of randomized placebo-controlled & open-label trials in patients with stable ischemic heart disease risk equivalents

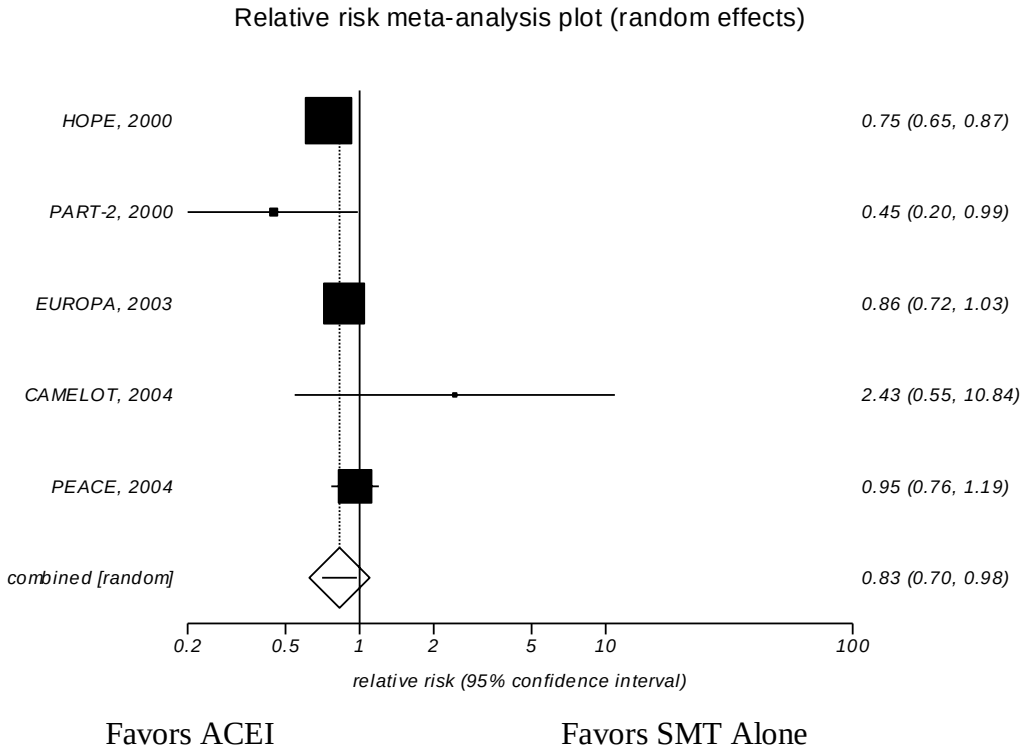


Test for heterogeneity: Cochran Q=4.461381 (df=1) p=0.0347
I^2 statistic=N/A

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 4. KQ1 Cardiovascular Mortality ACEI Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease

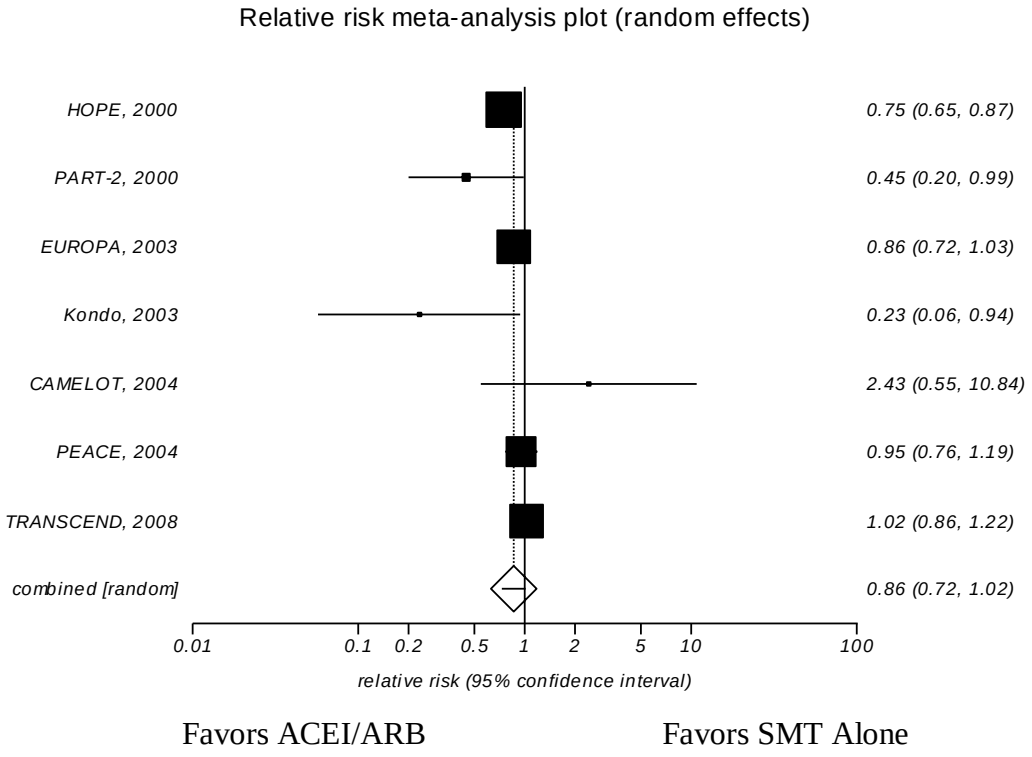


Test for heterogeneity: Cochran Q=7.343875 (df=4) p=0.1188
I^2 statistic=45.5%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 5. KQ1 Cardiovascular Mortality Sensitivity Analysis - Meta-analysis of randomized placebo-controlled or open-label trials in patients with stable ischemic heart disease

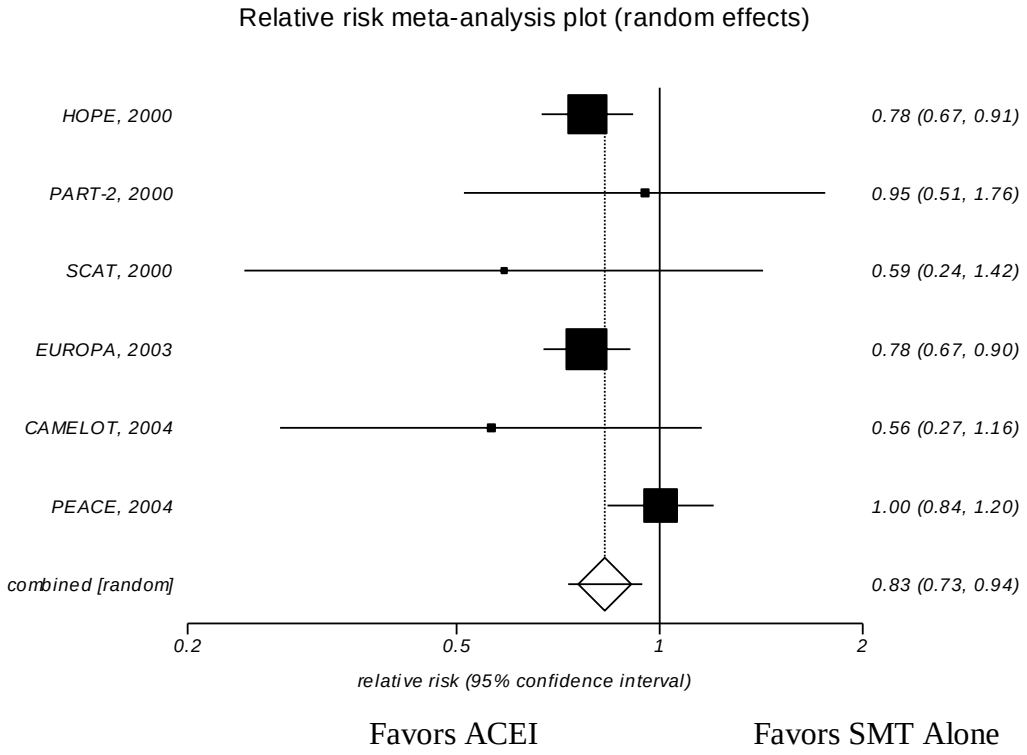


Test for heterogeneity: Cochran Q=14.733985 (df=6) p=0.0224
I^2 statistic=59.3%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 6. KQ1 Nonfatal Myocardial Infarction ACEI Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease

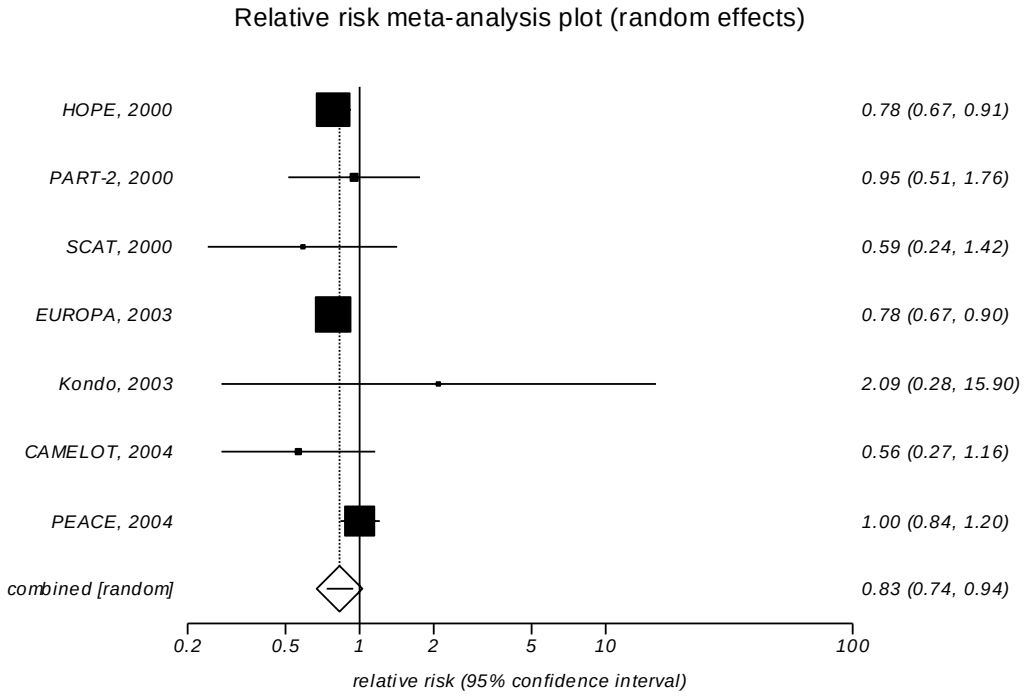


Test for heterogeneity: Cochran Q=7.189476 (df=5) p=0.2069
I^2 statistic=30.5%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 7. KQ1 Nonfatal Myocardial Infarction Sensitivity Analysis - Meta-analysis of randomized placebo-controlled + open-label trials in patients with stable ischemic heart disease



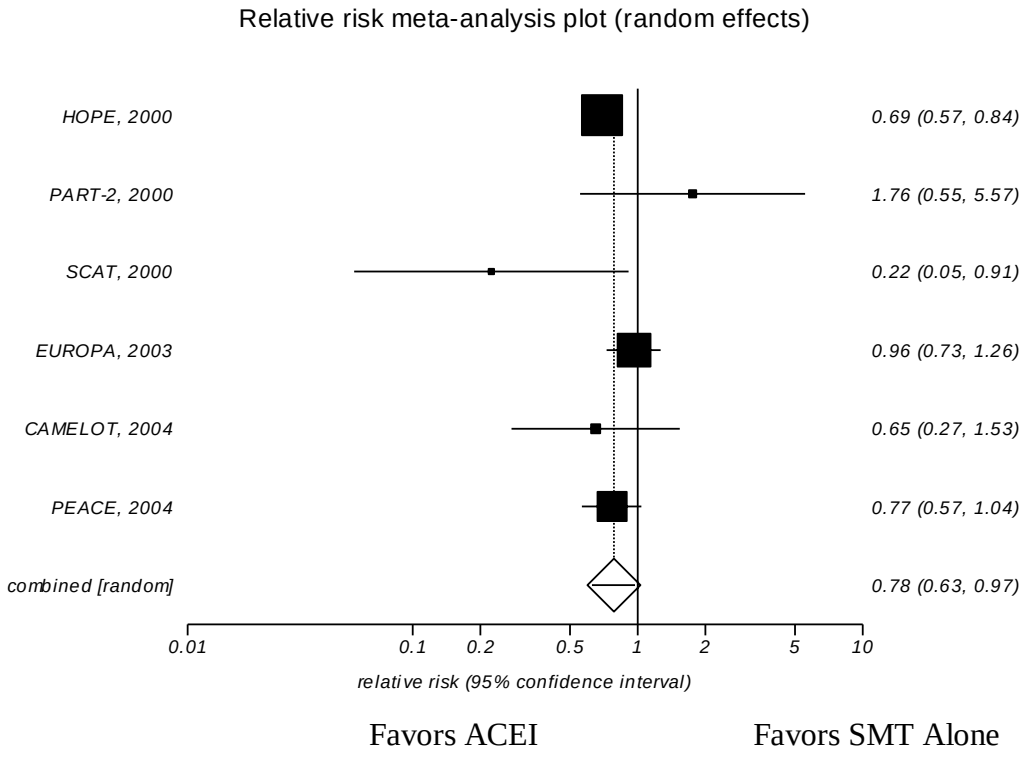
Favors ACEI/ARB Favors SMT Alone

Test for heterogeneity: Cochran Q=7.76543 (df=6) p=0.2558
I^2 statistic=22.7%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 8. KQ1 Stroke ACEI Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease

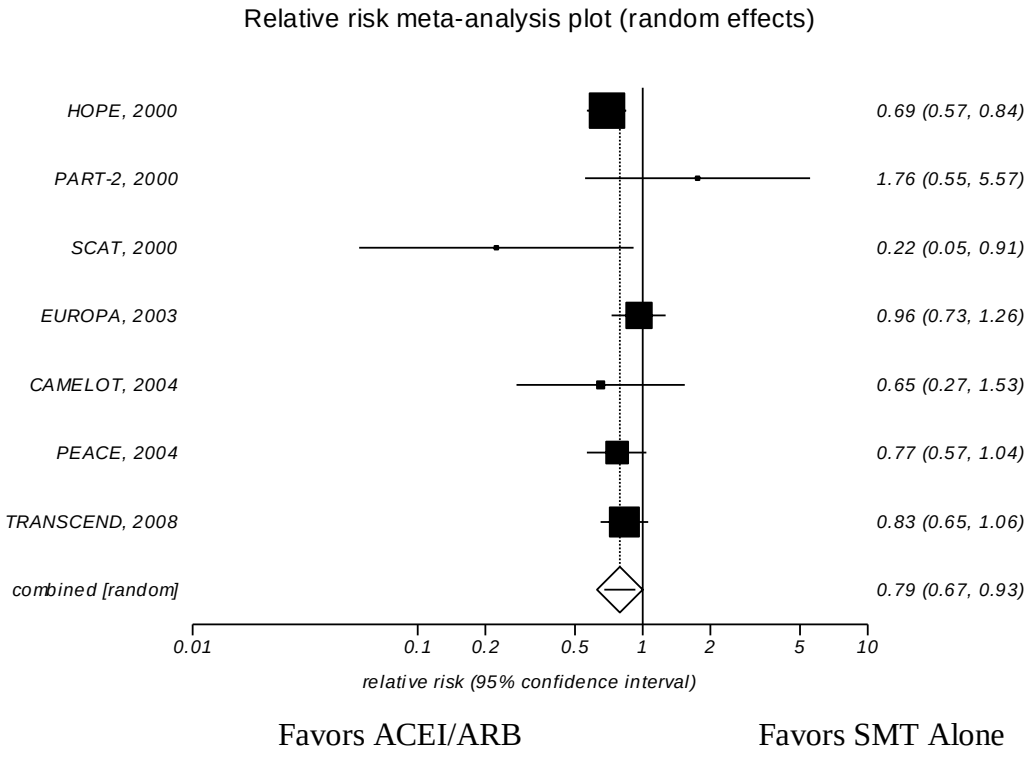


Test for heterogeneity: Cochran Q=8.03054 (df=5) p=0.1546
I^2 statistic=37.7%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 9. KQ1 Stroke Sensitivity Analysis - Meta-analysis of randomized placebo-controlled + open-label trials in patients with stable ischemic heart disease

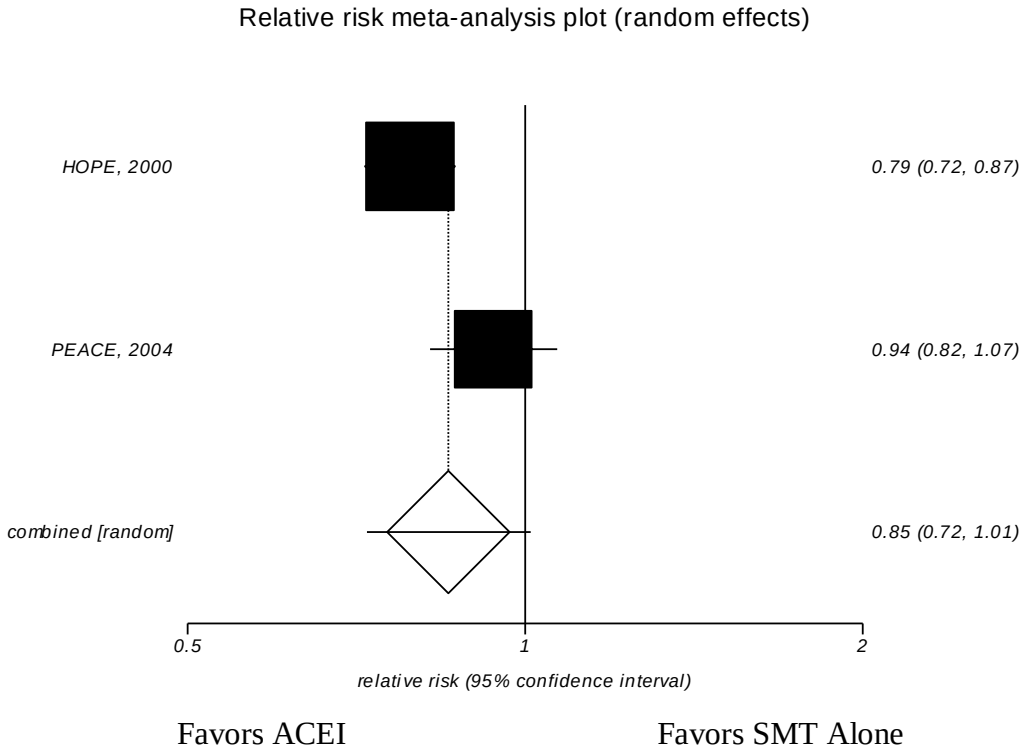


Test for heterogeneity: Cochran Q=8.291835 (df=6) p=0.011848
I^2 statistic=27.6%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 10. KQ1 composite of Cardiovascular Mortality, Nonfatal Myocardial Infarction and Stroke ACEI Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease

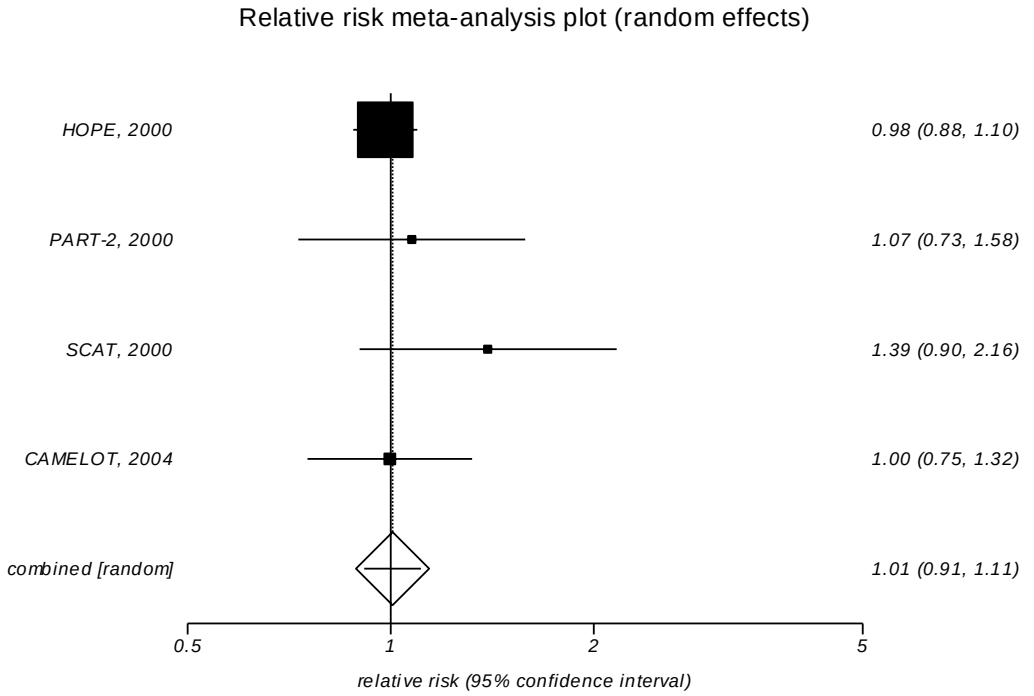


Test for heterogeneity: Cochran Q=4.365658 (df=1) p=0.0367
I^2 statistic=N/A

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 11. KQ1 Hospitalization For Angina ACEI Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease

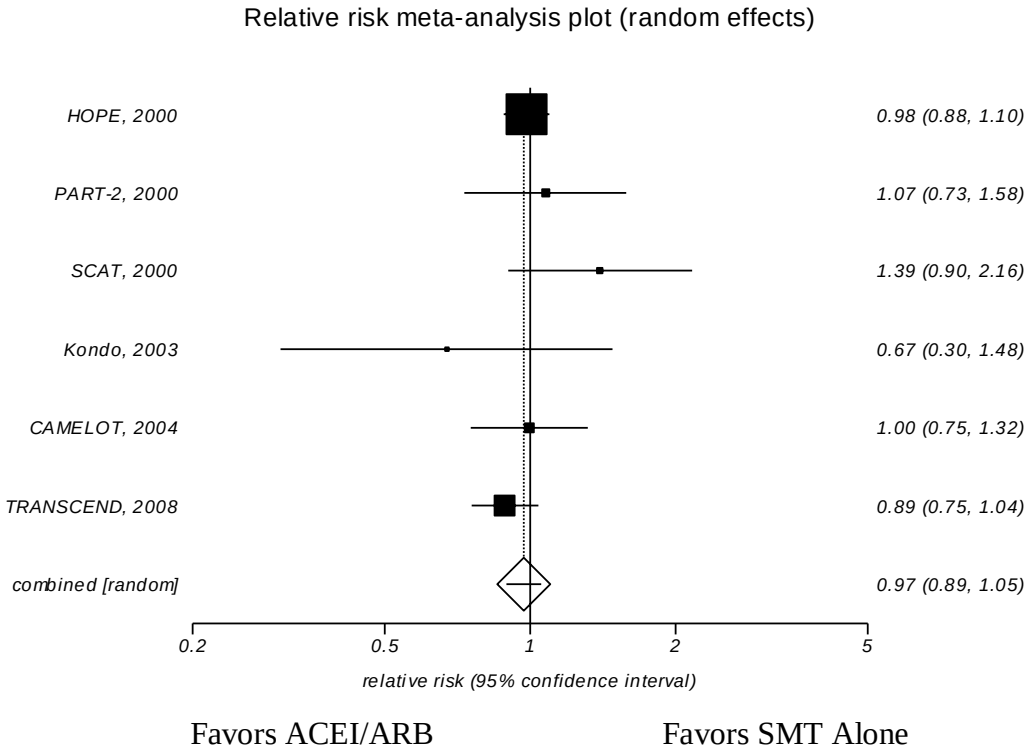


Test for heterogeneity: Cochran Q=2.371505 (df=3) p=0.499
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 12. KQ1 Hospitalization For Angina Sensitivity Analysis - Meta-analysis of randomized placebo-controlled + open-label trials in patients with stable ischemic heart disease

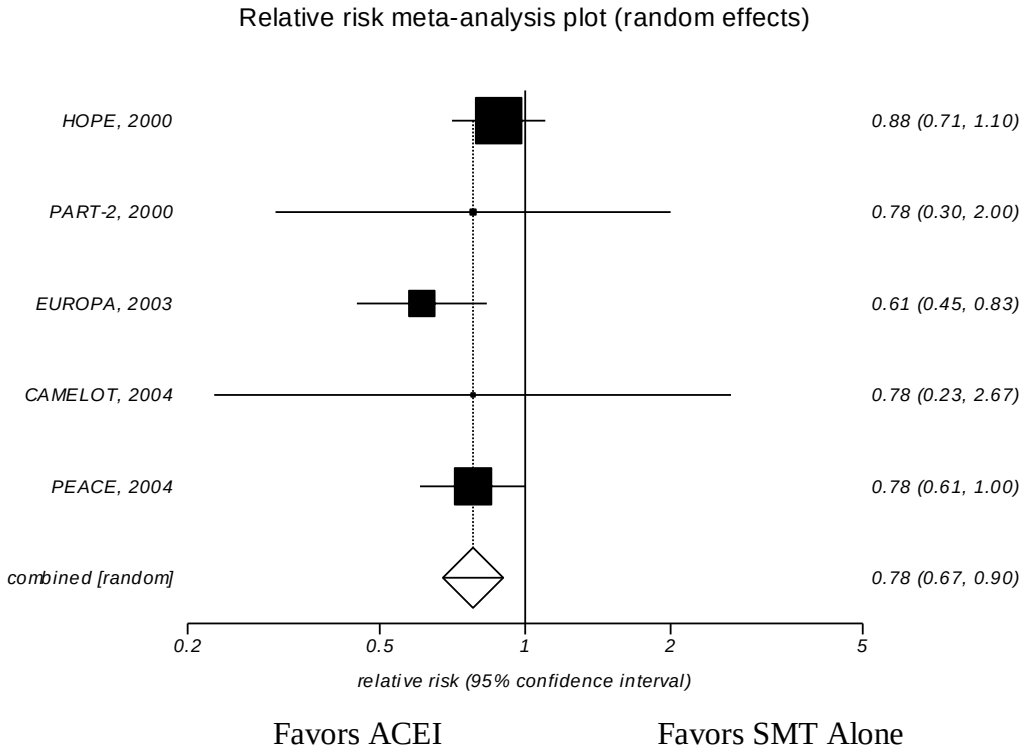


Test for heterogeneity: Cochran Q=4.876247 (df=5) p=0.4312
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 13. KQ1 Hospitalization For Heart Failure ACEI Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease

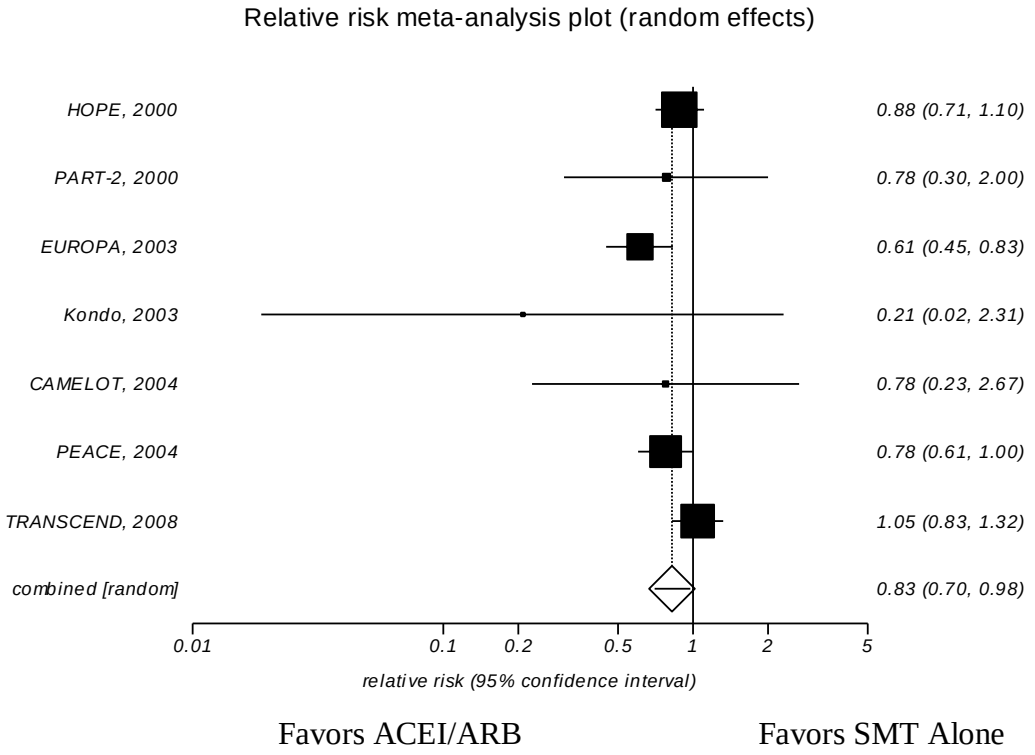


Test for heterogeneity: Cochran Q=3.530577 (df=4) p=0.4732
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 14. KQ1 Hospitalization For Heart Failure Sensitivity Analysis - Meta-analysis of randomized placebo-controlled + open-label trials in patients with stable ischemic heart disease

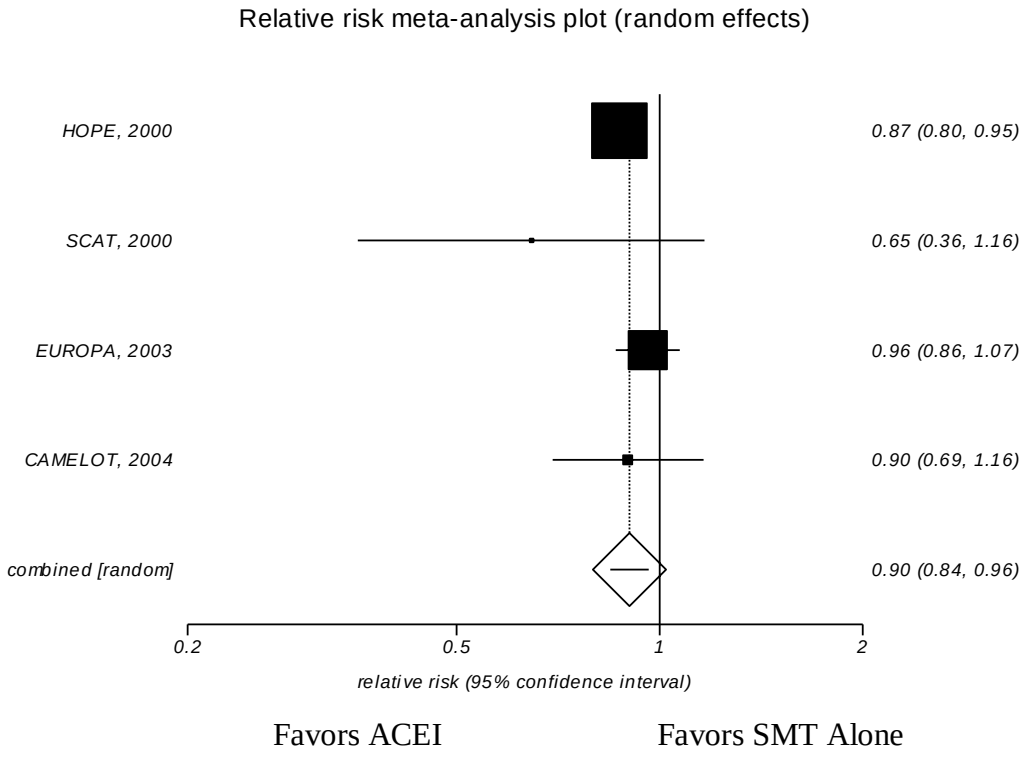


Test for heterogeneity: Cochran Q=8.660173 (df=6) p=0.1936
I^2 statistic=30.7%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 15. KQ1 Revascularization ACEI Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease

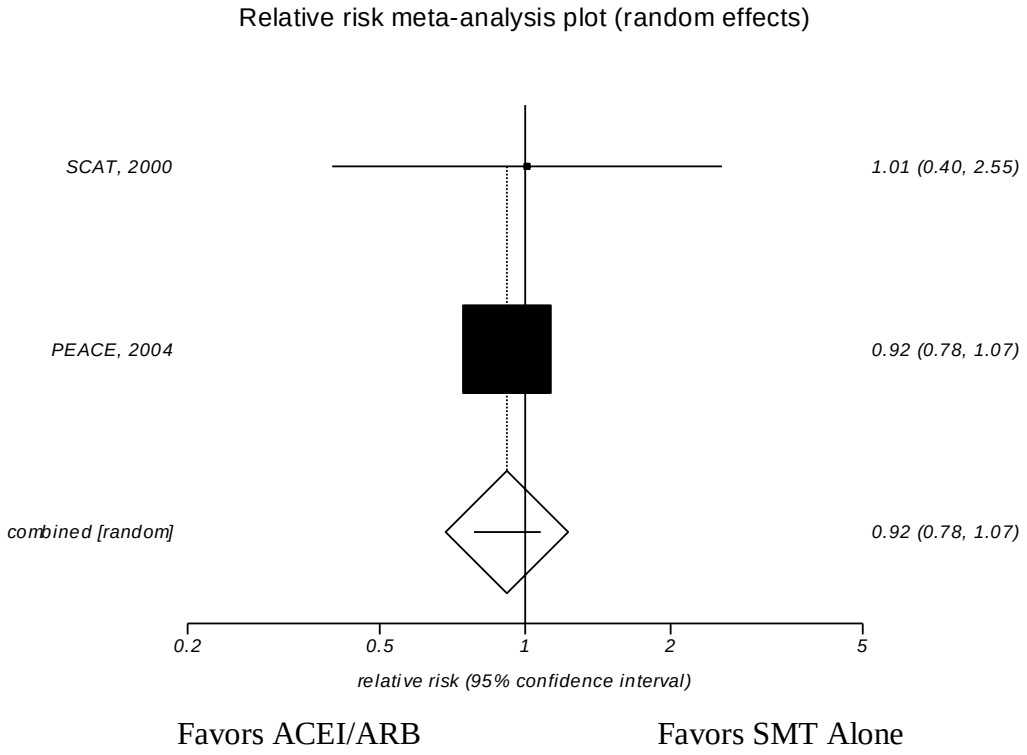


Test for heterogeneity: Cochran Q=2.989717 (df=3) p=0.3932
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 16. KQ1 Revascularization Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease undergoing coronary artery bypass grafting surgery only

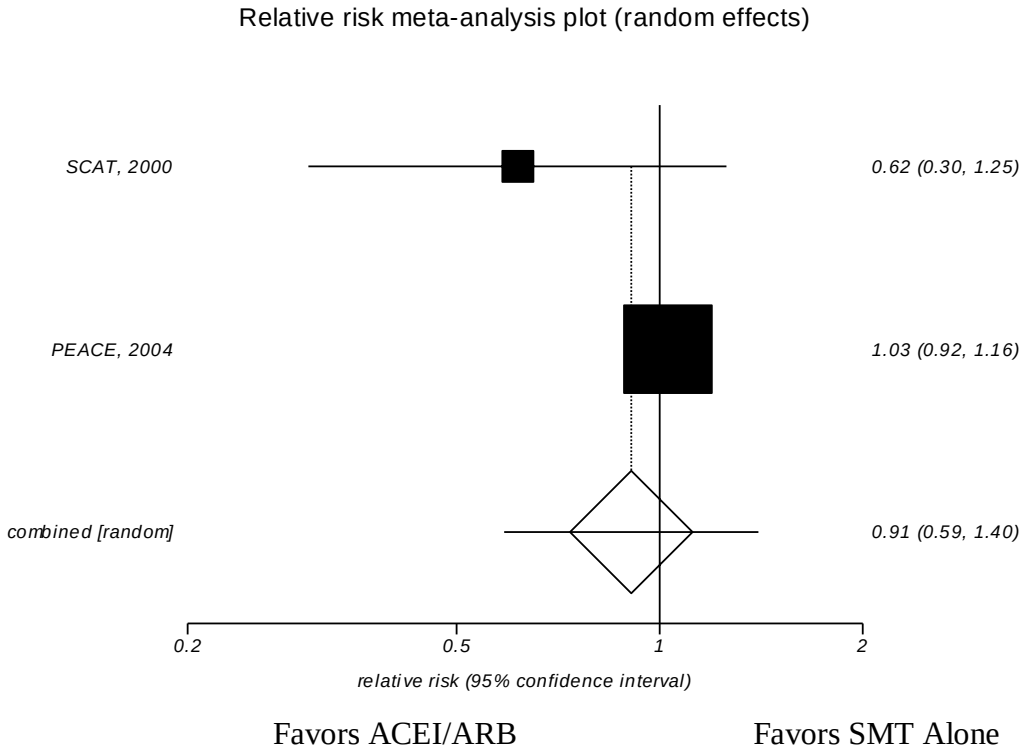


Test for heterogeneity: Cochran Q=0.037509 (df=1) p=0.8464
I^2 statistic=N/A

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 17. KQ1 Revascularization Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease undergoing percutaneous coronary intervention only

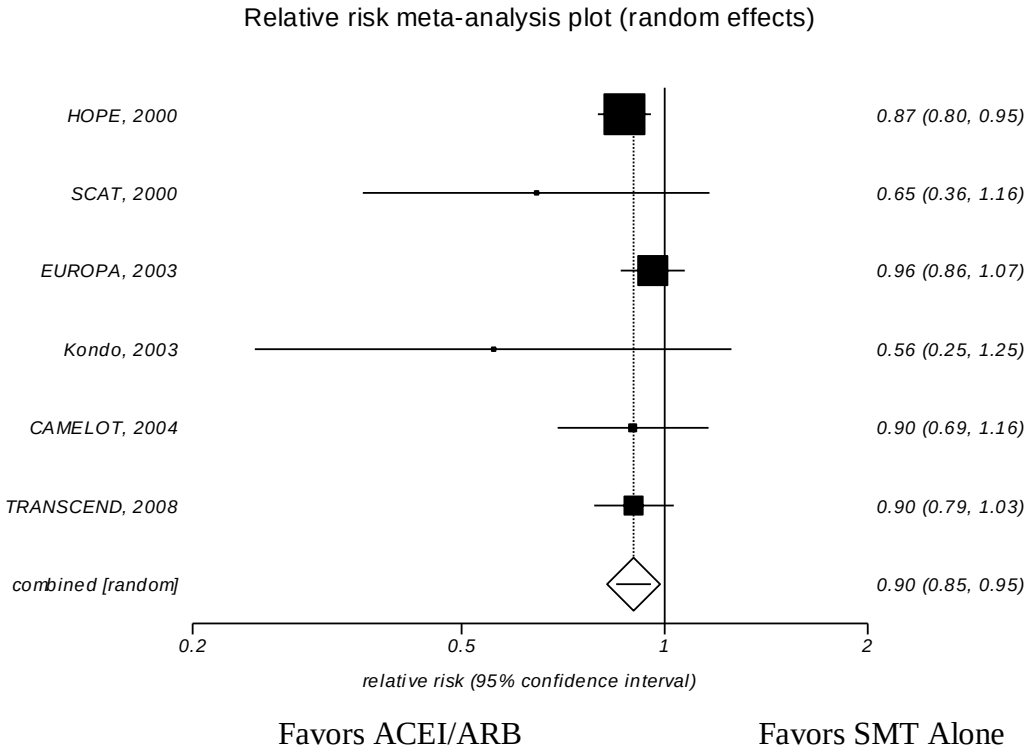


Test for heterogeneity: Cochran Q=1.864482 (df=1) p=0.1721
I^2 statistic=N/A

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 18. KQ1 Revascularization Sensitivity Analysis - Meta-analysis of randomized placebo-controlled or open-label trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=4.252035 (df=5) p=0.5137
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 12. KQ3 Total Mortality - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	Death	Cilazapril Placebo	7/1075 1/361	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	Mortality due to all causes	Ramipril Placebo	2/80 8/79	1-RR 76% (-1 to 92)
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	Total mortality	Quinapril Control	0/49 0/50	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	Deaths	Quinapril Placebo	0/46 0/45	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	All cause mortality	Quinapril Placebo	27/878 27/872	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	Deaths	Candesartan Placebo	0/63 0/57	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Death due to any cause	Quinapril Placebo	28/1280 28/1273	AHR 1.00 (0.59 to 1.69)

† Outcomes provided by personal communication with corresponding author

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 13. KQ3 Cardiovascular Mortality - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	CV death, including cardiac death and fatal stroke	Ramipril Placebo	1/80 8/79	1-RR 88% (24 to 94)
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	Cardiovascular death	Quinapril Control	0/49 0/50	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	Deaths‡	Quinapril Placebo	0/46 0/45	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	CV death, including cardiac death and vascular/stroke death	Quinapril Placebo	13/878 14/872	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	Deaths‡	Candesartan Placebo	0/63 0/57	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Cardiovascular death	Quinapril Placebo	18/1280 15/1273	AHR 1.20 (0.60 to 2.38)

† Outcomes provided by personal communication with corresponding author; ‡ No deaths occurred during the study.

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 14. KQ3 Nonfatal Myocardial Infarction - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	Nonfatal MI	Cilazapril Placebo	27/1075 8/361	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%; 5-7 days prior to randomization) or PTCA (18%; 1-2 days prior to randomization) for angina	NR	Ramipril Placebo	NR	NR
Kondo et al, 2001[55]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	Nonfatal MI	Quinapril Placebo	1/46 0/45	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	Nonfatal MI defined as changes in 1 or more of three parameters: symptomatology, enzyme elevation and ECG changes	Quinapril Placebo	36/878 40/872	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	Nonfatal MI†	Candesartan Placebo	1/63 2/57	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Nonfatal MI	Quinapril Placebo	16/1280 21/1273	AHR 0.76 (0.40 to 1.46)

† AACHEN reported no deaths in the trial, with one MI in the Candesartan group and two in the placebo group therefore events were entered as nonfatal.

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 15. KQ3 Stroke - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%)(5-7 days prior to randomization) or PTCA (18%)(1-2 days prior to randomization) for angina	Fatal stroke	Ramipril Placebo	0/80 1/79	NR
Kondo et al, 2001[55]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Stroke	Quinapril Placebo	15/1280 14/1273	AHR 1.07 (0.52 to 2.21)

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 16. KQ3 Composite: Cardiovascular Mortality, Nonfatal Myocardial Infarction, or Stroke - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	Cilazapril Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%)(5-7 days prior to randomization) or PTCA (18%)(1-2 days prior to randomization) for angina	Ramipril Placebo	NR	NR
Kondo et al, 2001[55]	RCT	Received elective balloon angioplasty followed by coronary stenting	Quinapril Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	Quinapril Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	Quinapril Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	Candesartan Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Quinapril Placebo	45/1280 45/1273	AHR 1.00 (0.66 to 1.51)

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 17. KQ3 Atrial Fibrillation - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%)(5-7 days prior to randomization) or PTCA (18%)(1-2 days prior to randomization) for angina	NR	Ramipril Placebo	NR	NR
Kondo et al, 2001[55†]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	New-onset atrial fibrillation (after randomization)	Quinapril Placebo	114/1280 101/1273	% risk difference 1 (-1.2 to 3.1)

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 18. KQ3 Hospitalization For Angina - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%)(5-7 days prior to randomization) or PTCA (18%)(1-2 days prior to randomization) for angina	Patients hospitalized with chest pain on suspicion of unstable angina	Ramipril Placebo	12/80 9/79	NR
Kondo et al, 2001[55]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	Patients hospitalized with unstable angina	Quinapril Placebo	45/878 52/872	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Hospitalization for unstable angina	Quinapril Placebo	45/1280 38/1273	AHR 1.19 (0.77 to 1.83)

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 19. KQ3 Hospitalization For Heart Failure - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%)(5-7 days prior to randomization) or PTCA (18%)(1-2 days prior to randomization) for angina	Hospitalization for heart failure	Ramipril Placebo	2/80 5/79	NR
Kondo et al, 2001[55]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Hospitalization for heart failure	Quinapril Placebo	15/1280 14/1273	AHR 1.09 (0.53 to 2.26)

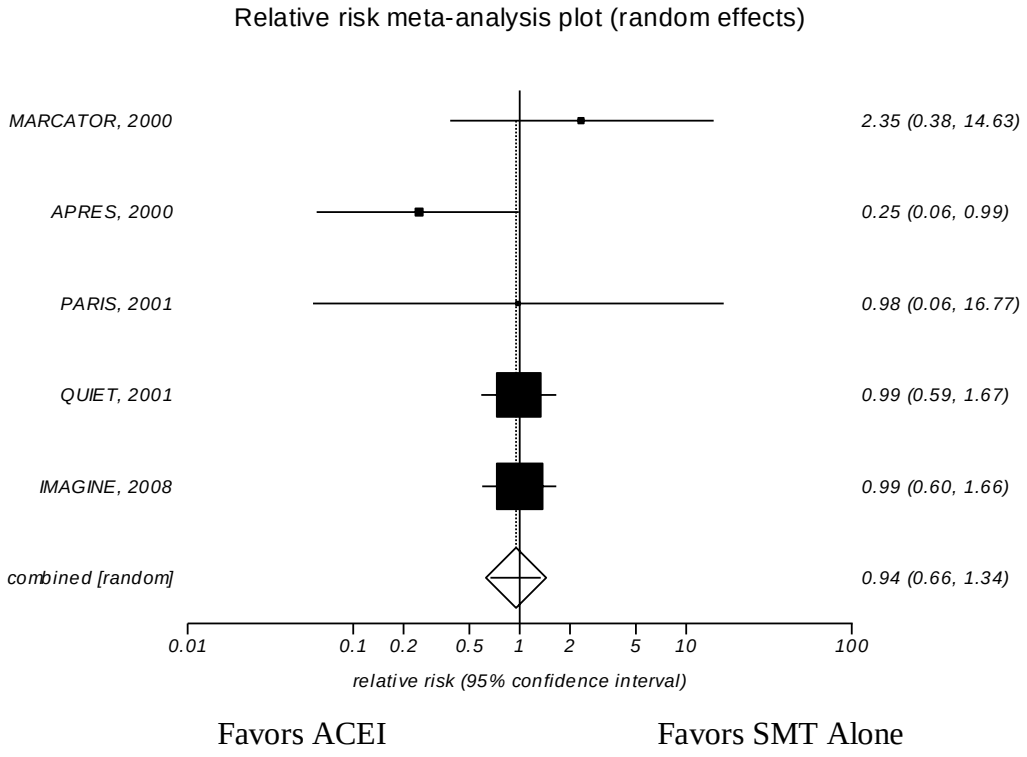
Appendix C: Additional Evidence Tables and Analyses

Appendix Table 20. KQ3 Revascularization - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	CABG or repeat angioplasty	Cilazapril Placebo	207/1075 54/361	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%)(5-7 days prior to randomization) or PTCA (18%)(1-2 days prior to randomization) for angina	NR	Ramipril Placebo	NR	NR
Kondo et al, 2001[55]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	Angioplasty or stent implantation	Quinapril Placebo	10/46 7/45	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	Coronary angioplasty	Quinapril Placebo	223/878 233/872	NR
			CABG	Quinapril Placebo	116/878 104/872	
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	Target lesion revascularization	Candesartan Placebo	5/63 4/57	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Coronary revascularization	Quinapril Placebo	52/1280 41/1273	AHR 1.28 (0.85 to 1.93)

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 19. KQ3 Total Mortality ACEI Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure

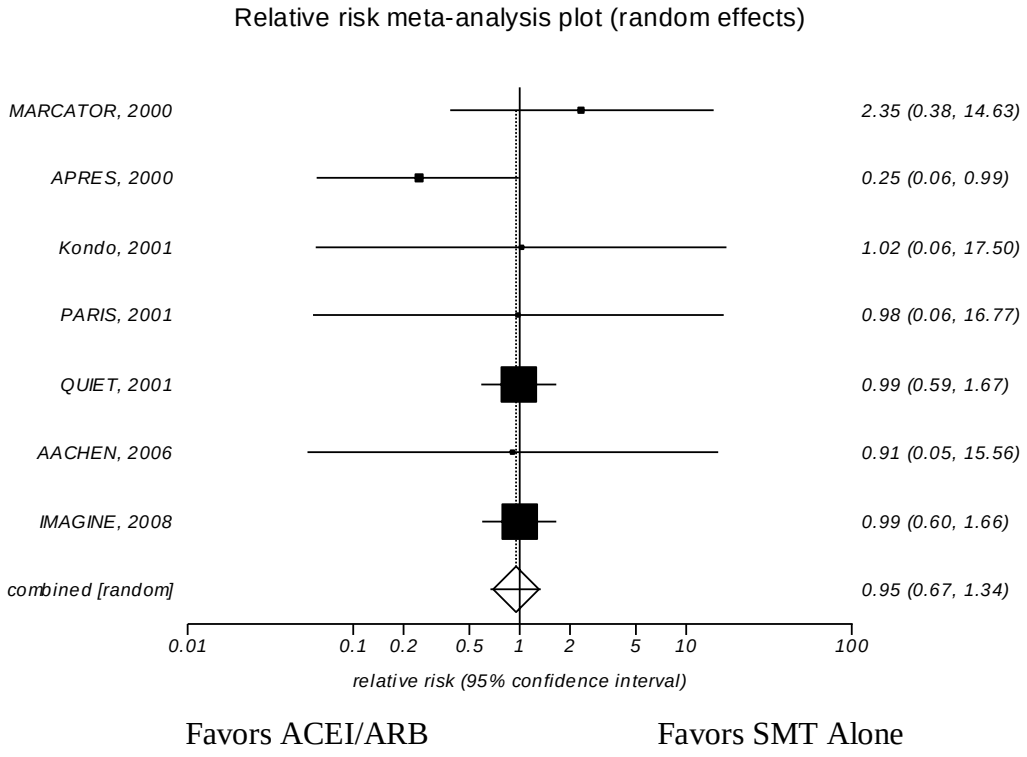


Test for heterogeneity: Cochran Q=3.810035 (df=4) p=0.4323
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 20. KQ3 Total Mortality Sensitivity Analysis - Meta-analysis of randomized placebo-controlled or open-label trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure

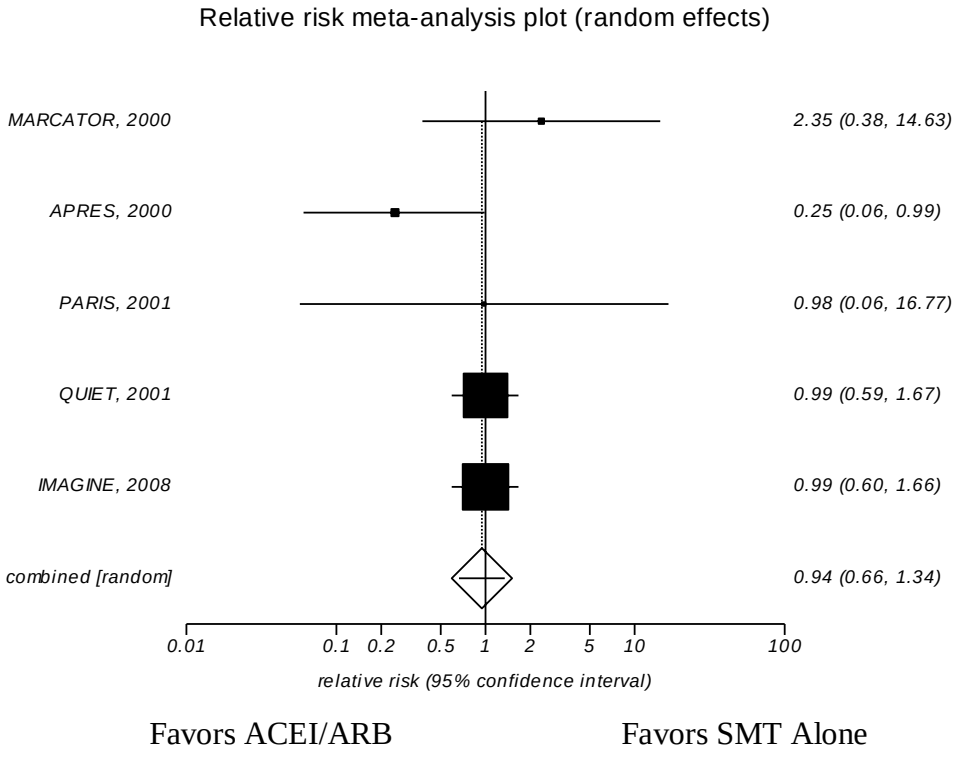


Test for heterogeneity: Cochran Q=3.811901 (df=6) p=0.7021
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 21. KQ3 Total Mortality Sensitivity Analysis - Meta-analysis of randomized placebo-controlled trials utilizing intention-to-treat methodologies in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure

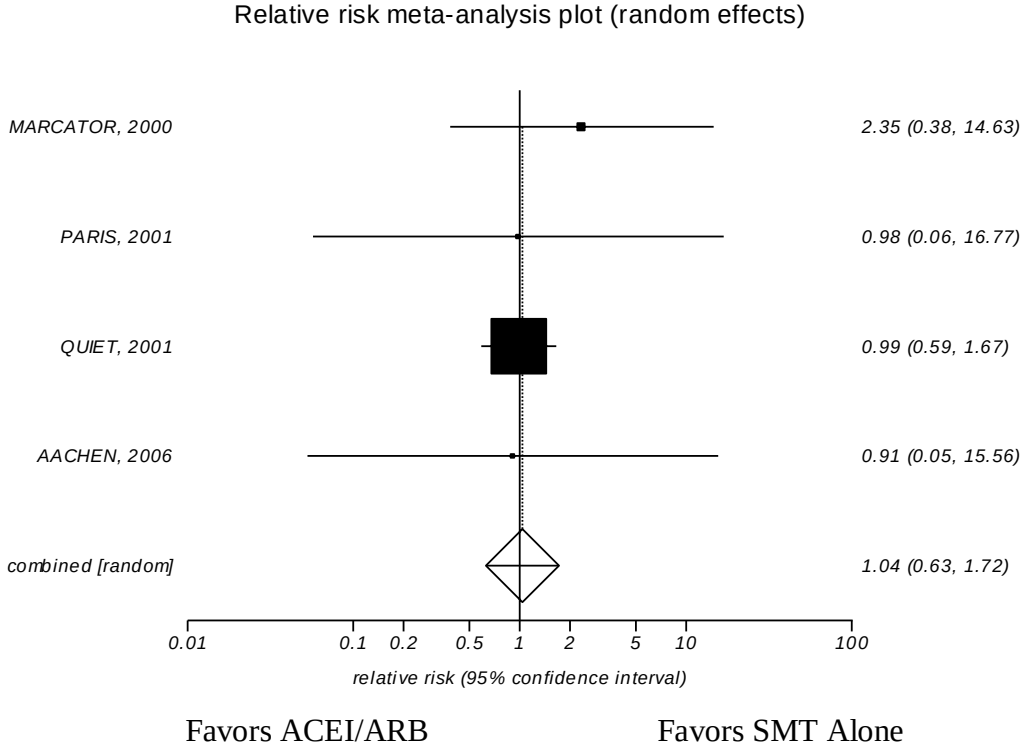


Test for heterogeneity: Cochran Q=3.810035 (df=4) p=0.4323
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 22. KQ3 Total Mortality Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, percutaneous procedure only

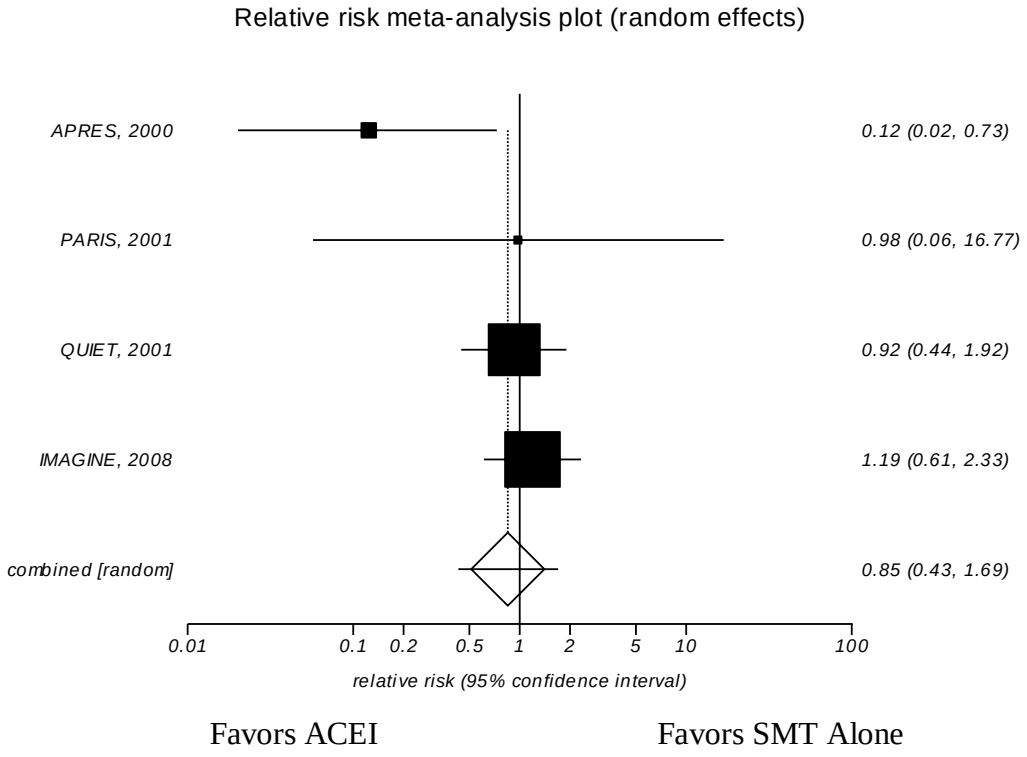


Test for heterogeneity: Cochran Q=0.623781 (df=3) p=0.891
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 23. KQ3 Cardiovascular Mortality ACEI Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure

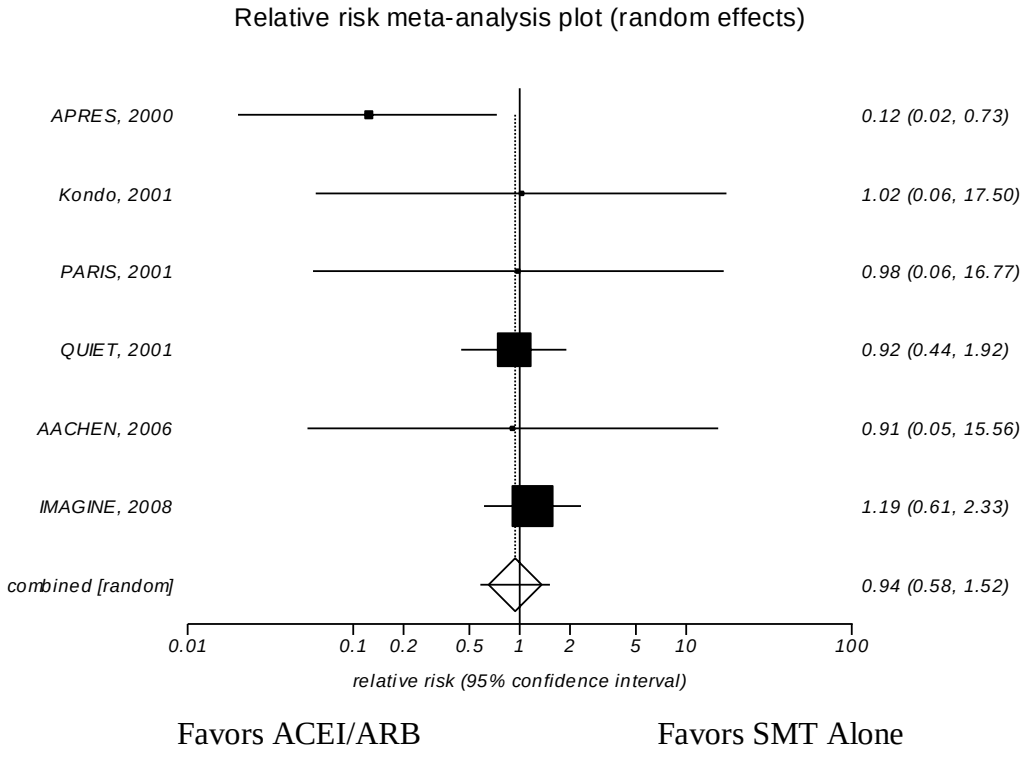


Test for heterogeneity: Cochran Q=4.351836 (df=3) p=0.2259
I^2 statistic=31.1%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 24. KQ3 Cardiovascular Mortality Sensitivity Analysis - Meta-analysis of randomized placebo-controlled or open-label trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure

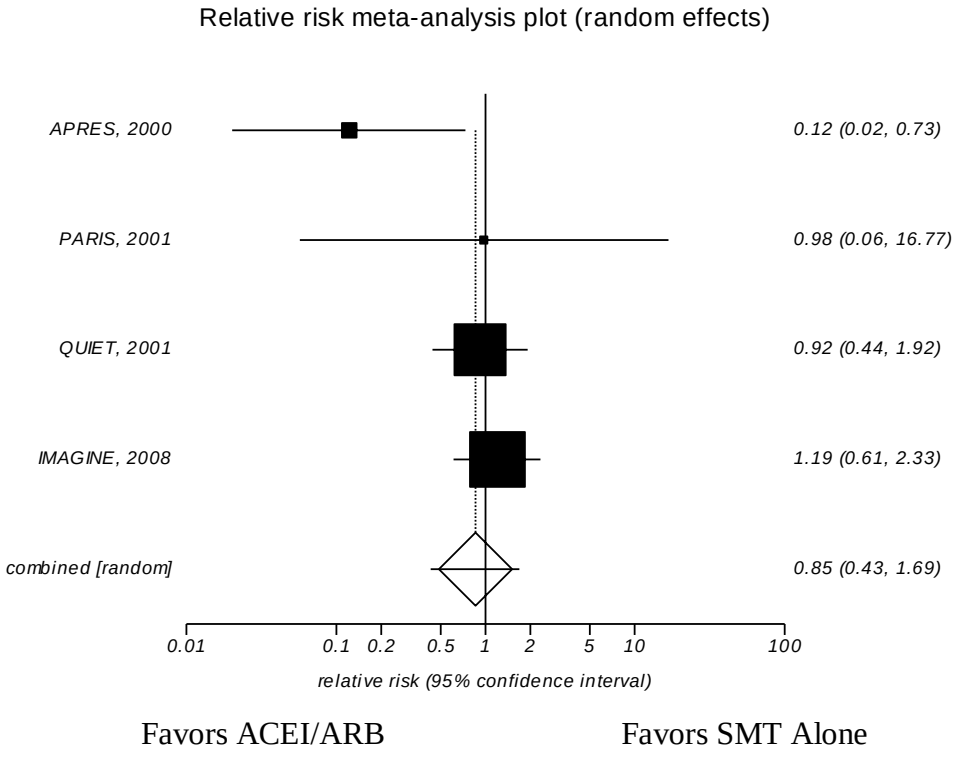


Test for heterogeneity: Cochran Q=4.350679 (df=5) p=0.5001
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 25. KQ3 Cardiovascular Mortality Sensitivity Analysis - Meta-analysis of randomized placebo-controlled trials utilizing intention-to-treat methodologies in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure

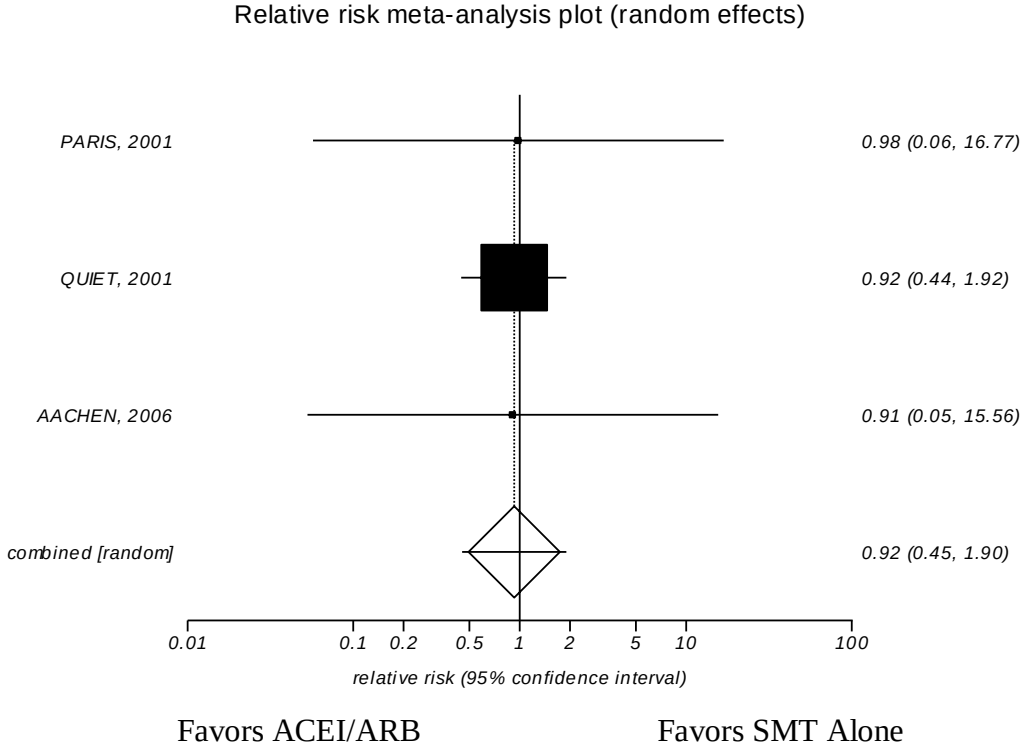


Test for heterogeneity: Cochran Q=4.351836 (df=3) p=0.2259
I^2 statistic=31.1%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 26. KQ3 Cardiovascular Mortality Sensitivity Analysis - Meta-analysis of randomized placebo-controlled or open-label trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, percutaneous procedure only

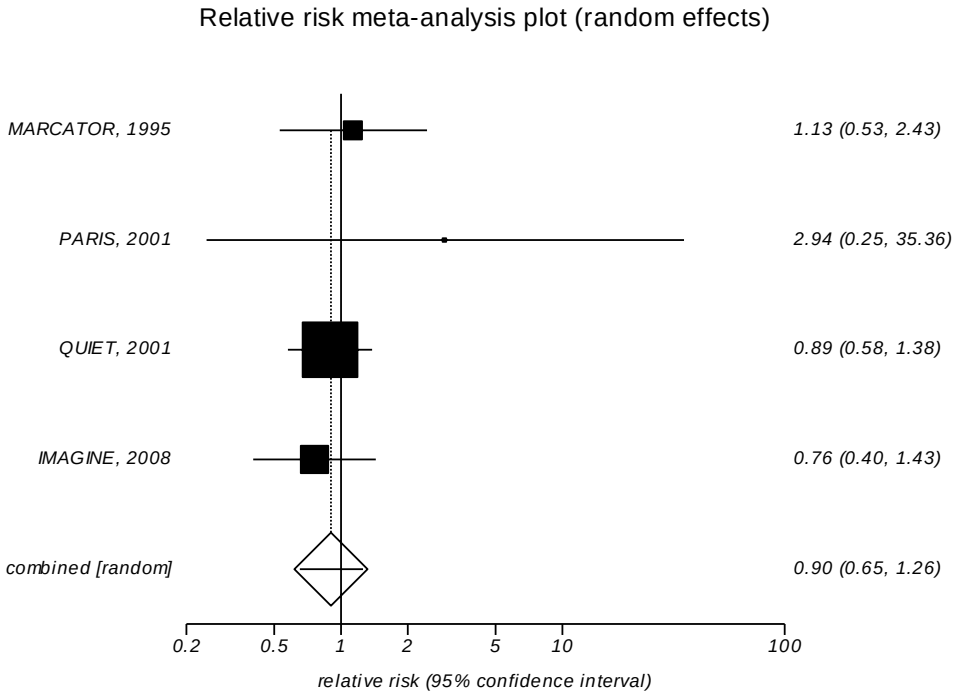


Test for heterogeneity: Cochran Q=0.000956 (df=2) p=0.9995
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 27. KQ3 Nonfatal Myocardial Infarction ACEI Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



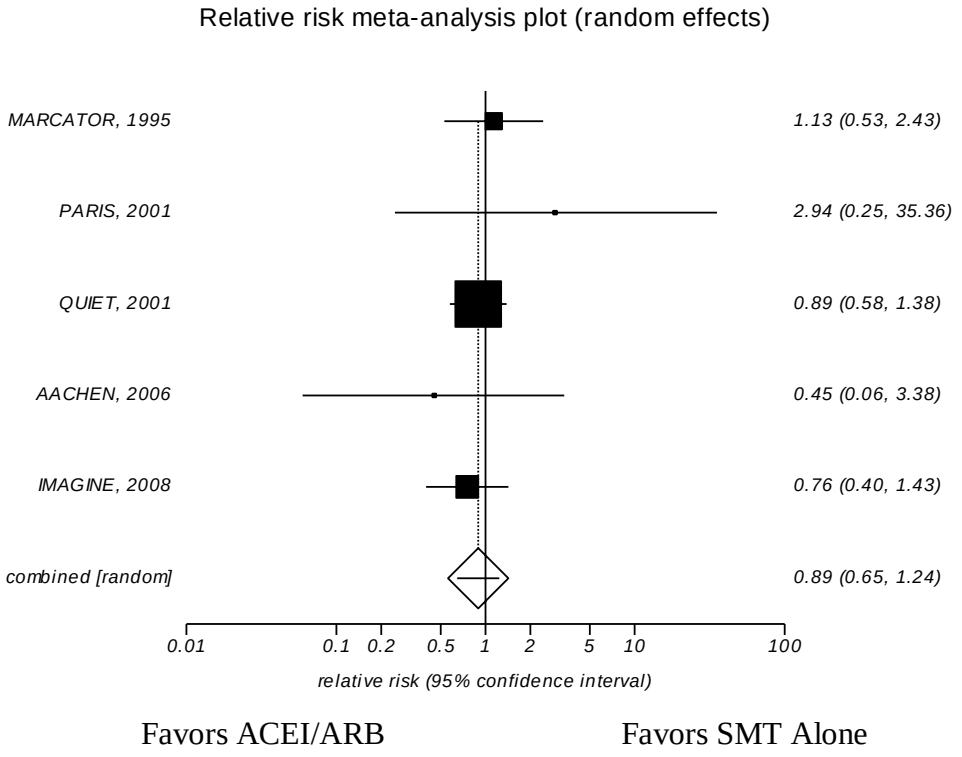
Favors ACEI Favors SMT Alone

Test for heterogeneity: Cochran Q=1.11656 (df=3) p=0.767
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 28. KQ3 Nonfatal Myocardial Infarction Sensitivity Analysis - Meta-analysis of randomized placebo-controlled + open-label trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure

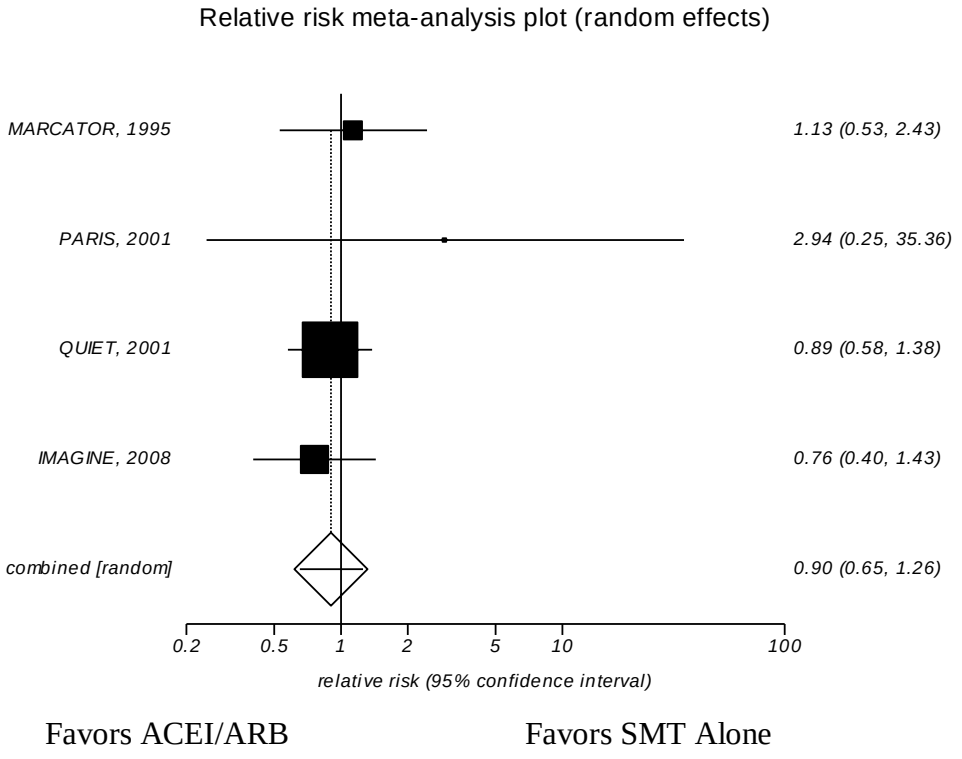


Test for heterogeneity: Cochran Q=1.46284 (df=4) p=0.8332
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 29. KQ3 Nonfatal Myocardial Infarction Sensitivity Analysis - Meta-analysis of randomized placebo-controlled trials utilizing intention-to-treat methodologies in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure

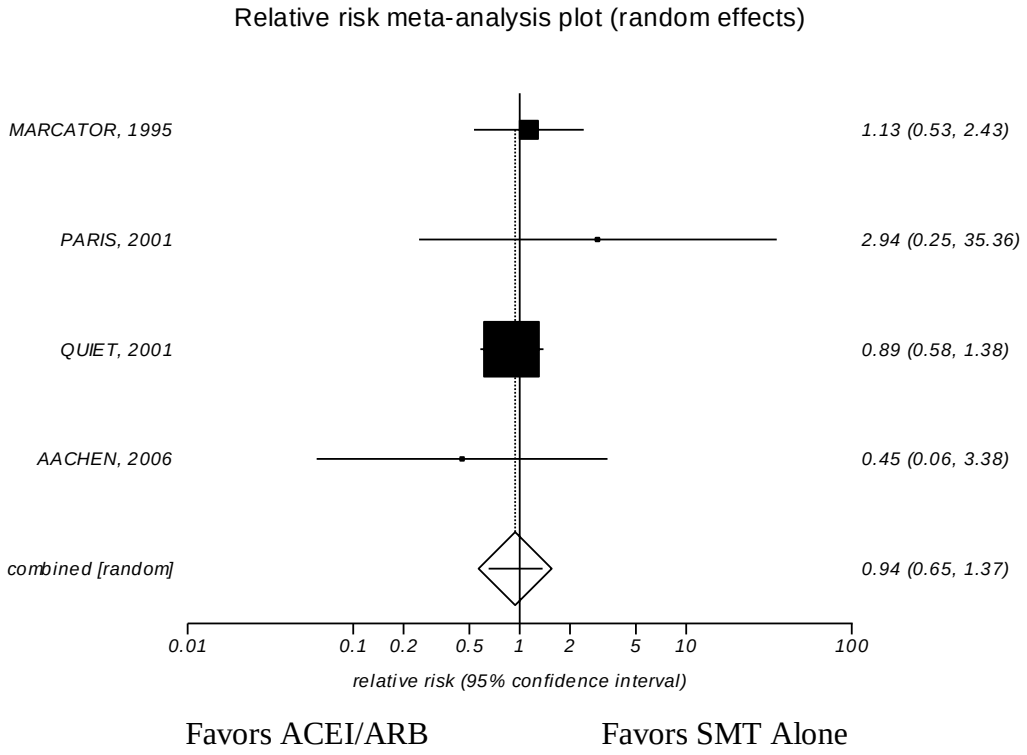


Test for heterogeneity: Cochran Q=1.141656 (df=3) p=0.767
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 30. KQ3 Nonfatal Myocardial Infarction Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, percutaneous procedure only

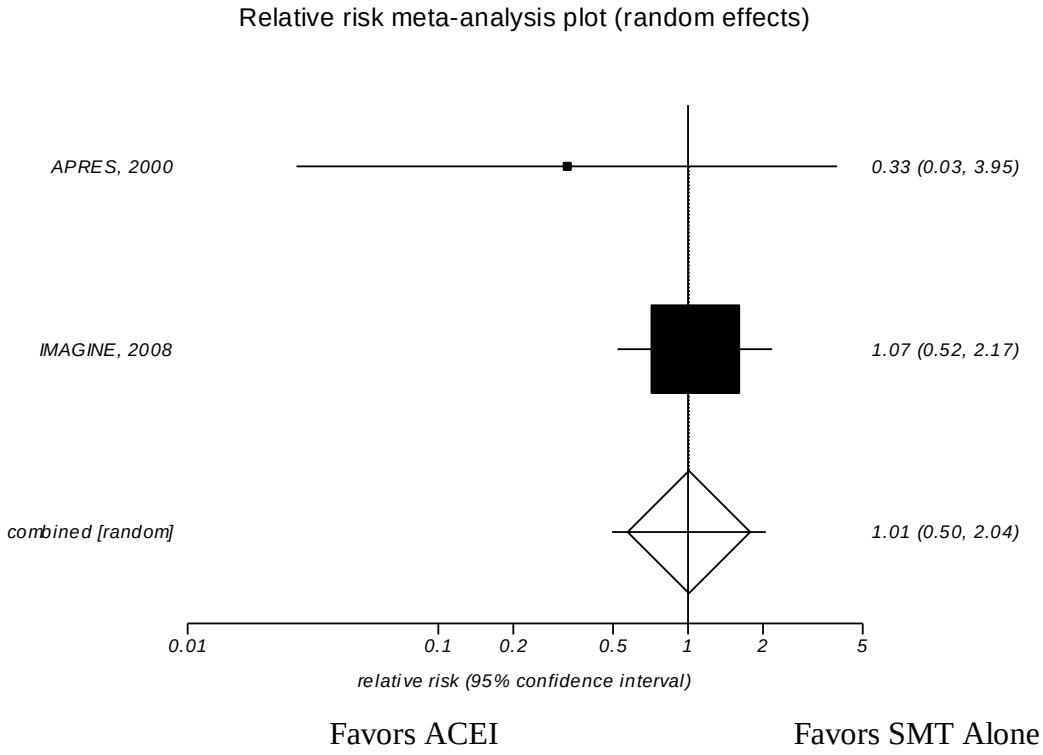


Test for heterogeneity: Cochran Q=1.130237 (df=3) p=0.7698
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 31. KQ3 Stroke ACEI Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure

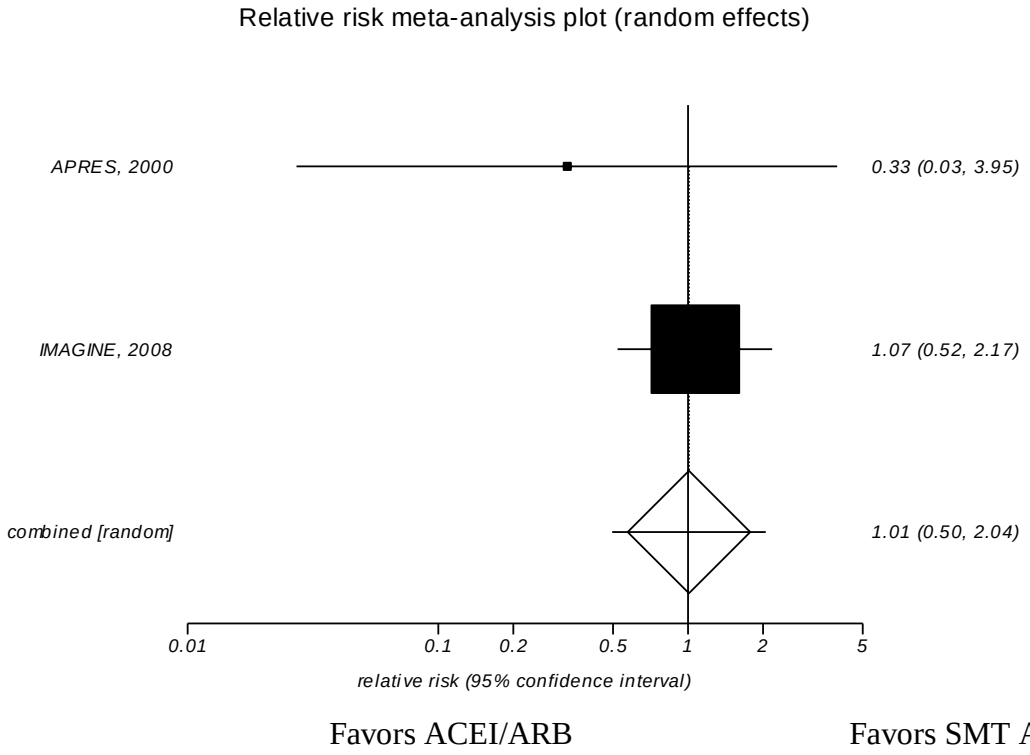


Test for heterogeneity: Cochran Q=0.497689 (df=1) p=0.4805
I^2 statistic=N/A

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 32. KQ3 Stroke Sensitivity Analysis - Meta-analysis of randomized placebo-controlled or open-label trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure

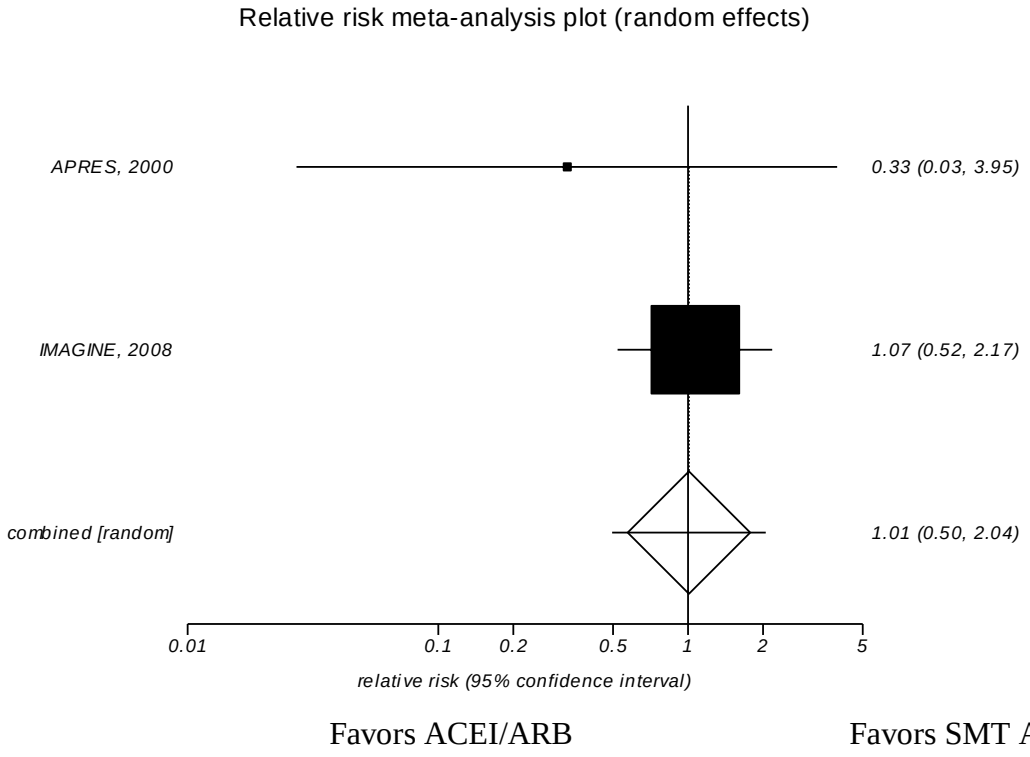


Test for heterogeneity: Cochran Q=0.497689 (df=1) p=0.4805
I^2 statistic=N/A

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 33. KQ3 Stroke Sensitivity Analysis - Meta-analysis of randomized placebo-controlled trials utilizing intention-to-treat methodologies in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure

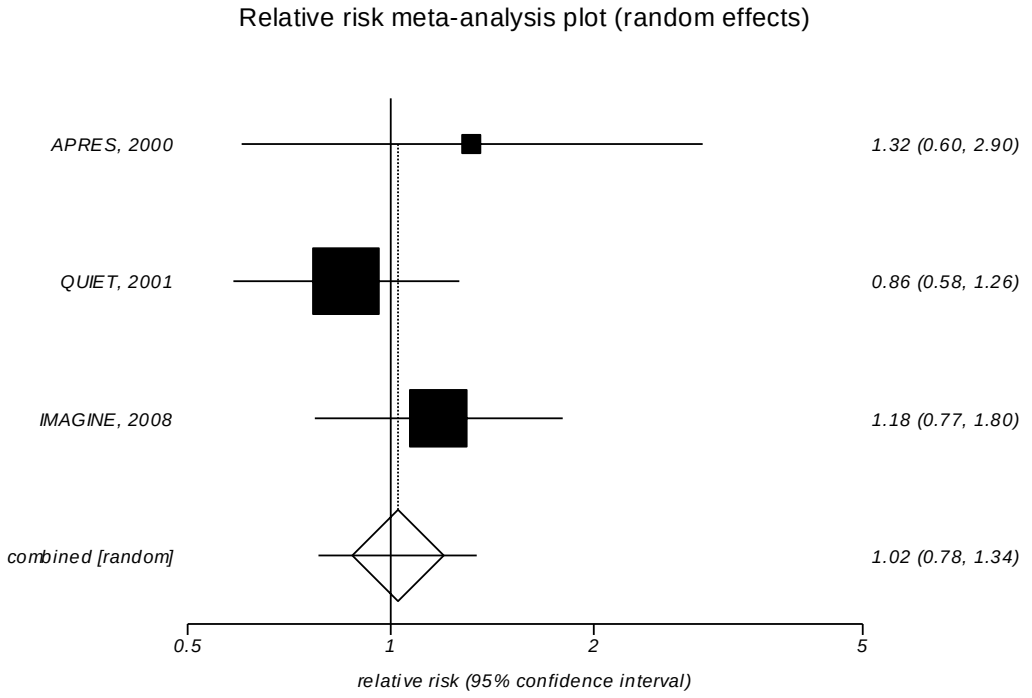


Test for heterogeneity: Cochran Q=0.497689 (df=1) p=0.4805
I^2 statistic=N/A

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 34. KQ3 Hospitalization For Angina ACEI Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



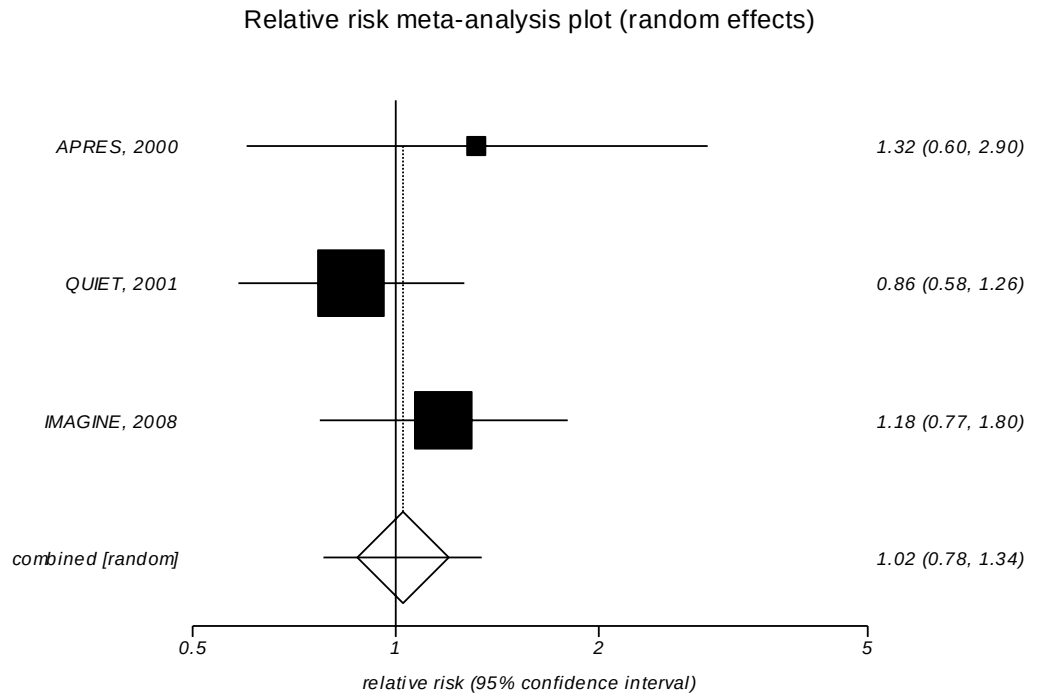
Favors ACEI Favors SMT Alone

Test for heterogeneity: Cochran Q=1.573147 (df=2) p=0.4554
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 35. KQ3 Hospitalization For Angina Sensitivity Analysis - Meta-analysis of randomized placebo-controlled or open-label trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



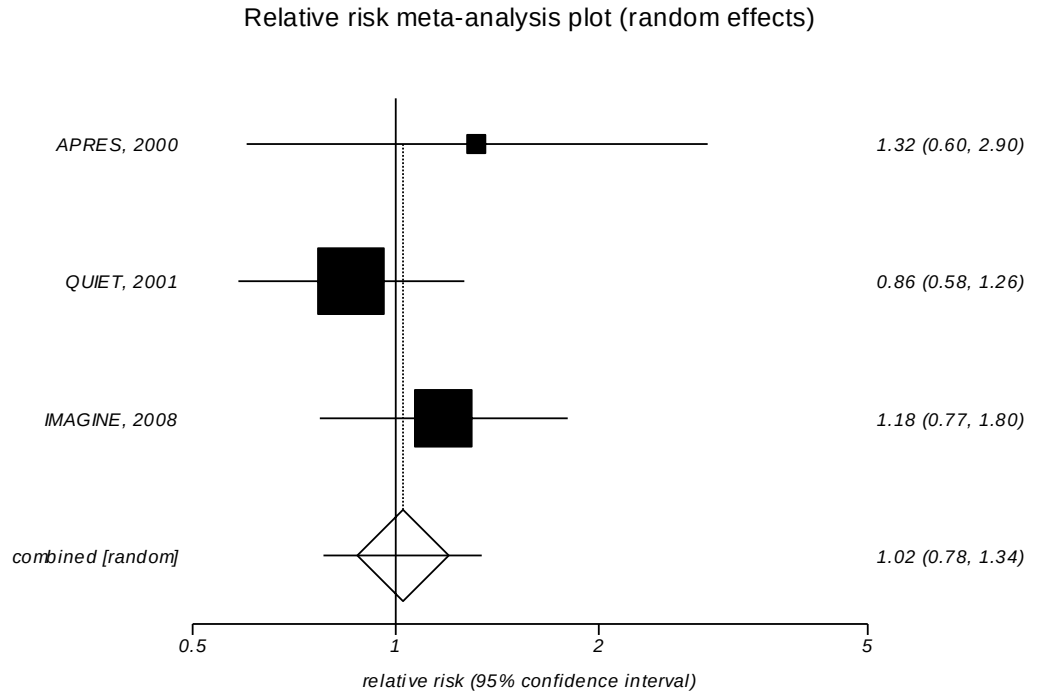
Favors ACEI/ARB Favors SMT Alone

Test for heterogeneity: Cochran Q=1.573147 (df=2) p=0.4554
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 36. KQ3 Hospitalization For Angina Sensitivity Analysis - Meta-analysis of randomized placebo-controlled trials utilizing intention-to-treat methodologies in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure



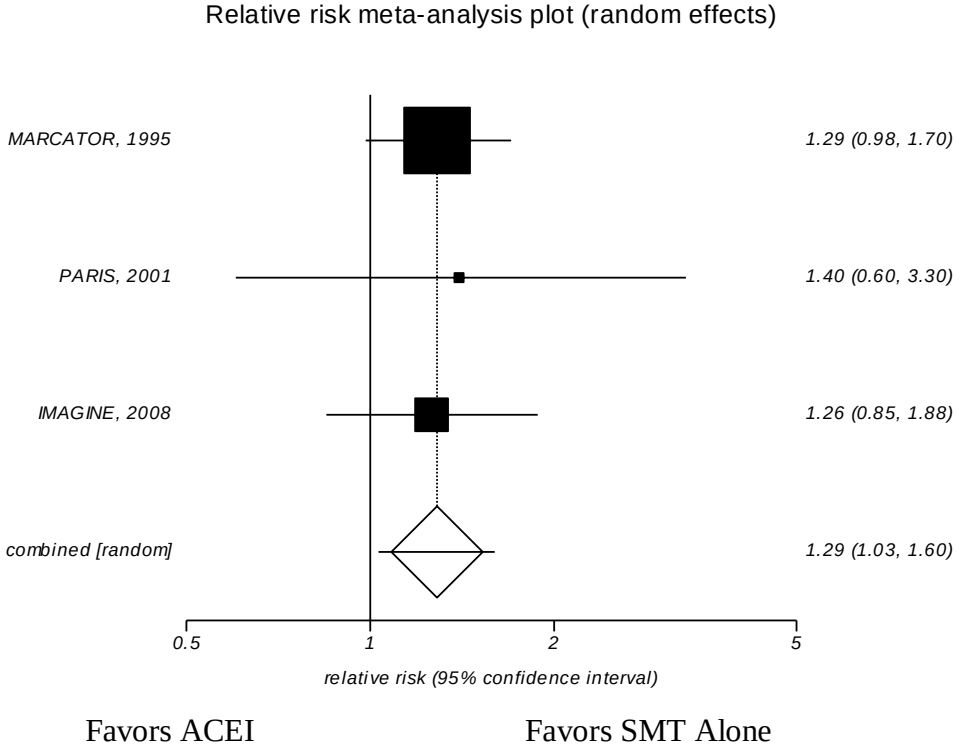
Favors ACEI/ARB Favors SMT Alone

Test for heterogeneity: Cochran Q=1.573147 (df=2) p=0.4554
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 37. KQ3 Revascularizations ACEI Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure

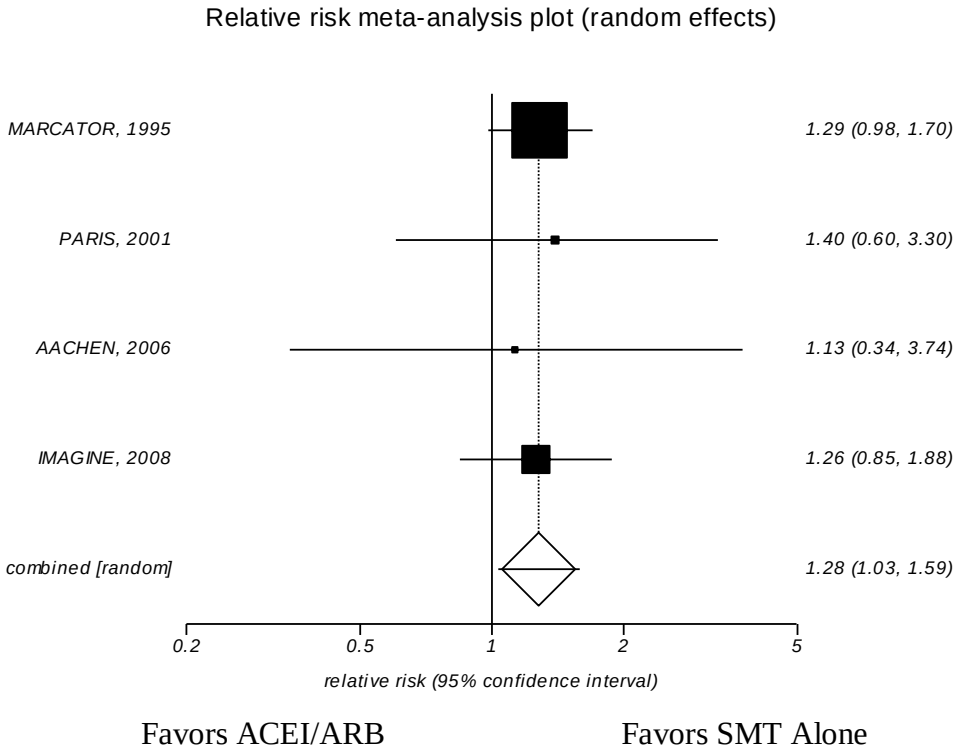


Test for heterogeneity: Cochran Q=0.043777 (df=2) p=0.9783
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 38. KQ3 Revascularizations Sensitivity Analysis - Meta-analysis of randomized placebo-controlled or open-label trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure

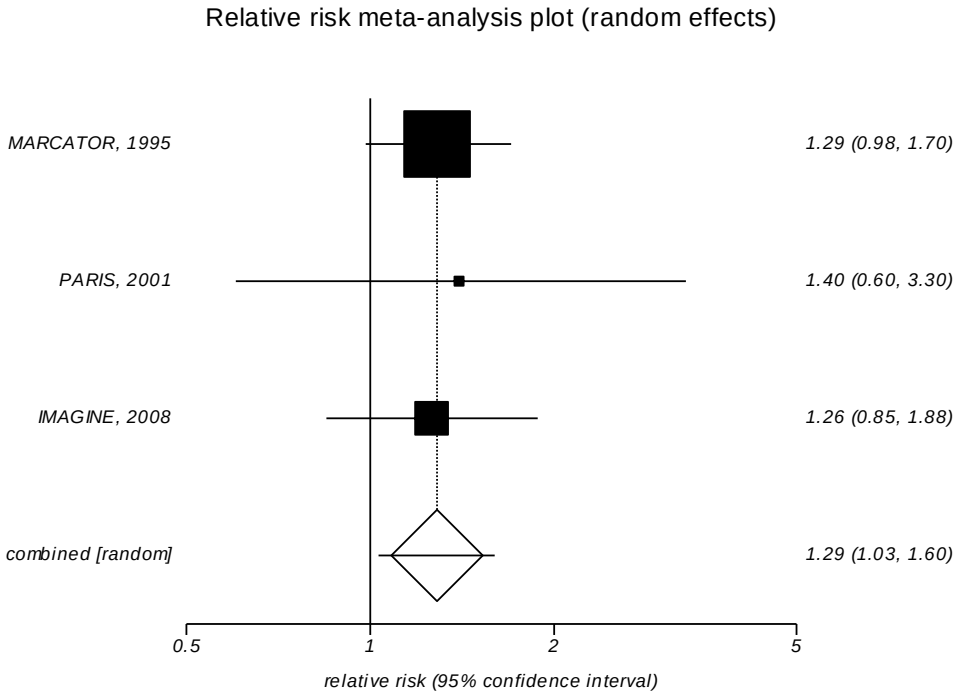


Test for heterogeneity: Cochran Q=0.082314 (df=3) p=0.9939
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 39. KQ3 Revascularizations Sensitivity Analysis - Meta-analysis of randomized placebo-controlled trials utilizing intention-to-treat methodologies in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, a coronary revascularization procedure

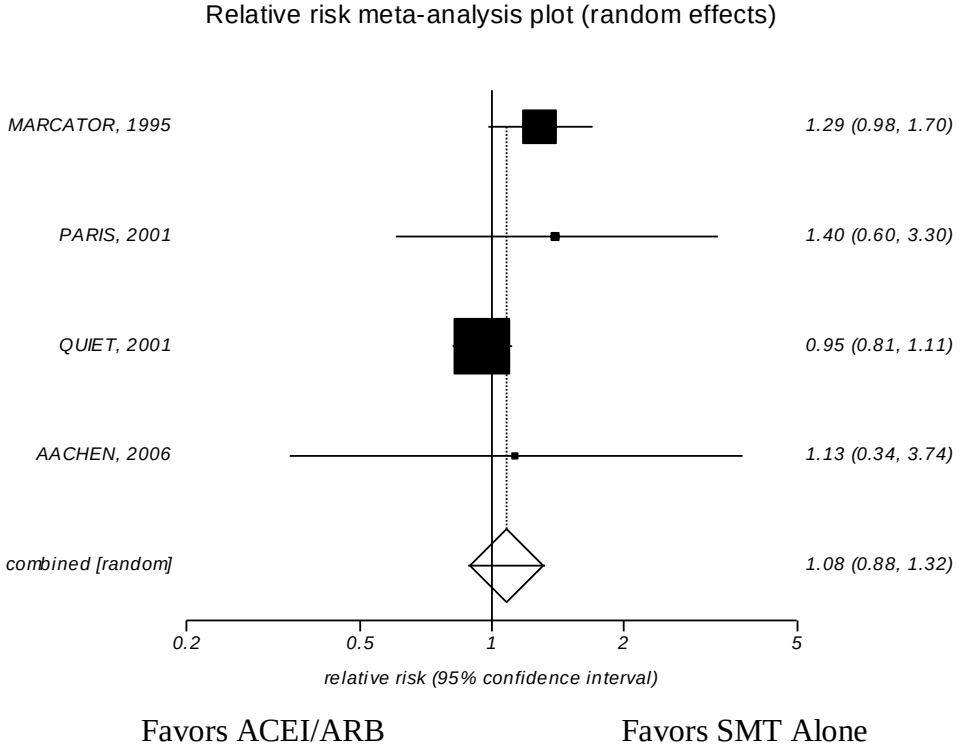


Test for heterogeneity: Cochran Q=0.043777 (df=2) p=0.9783
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 40. KQ3 Revascularizations Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, percutaneous procedure only

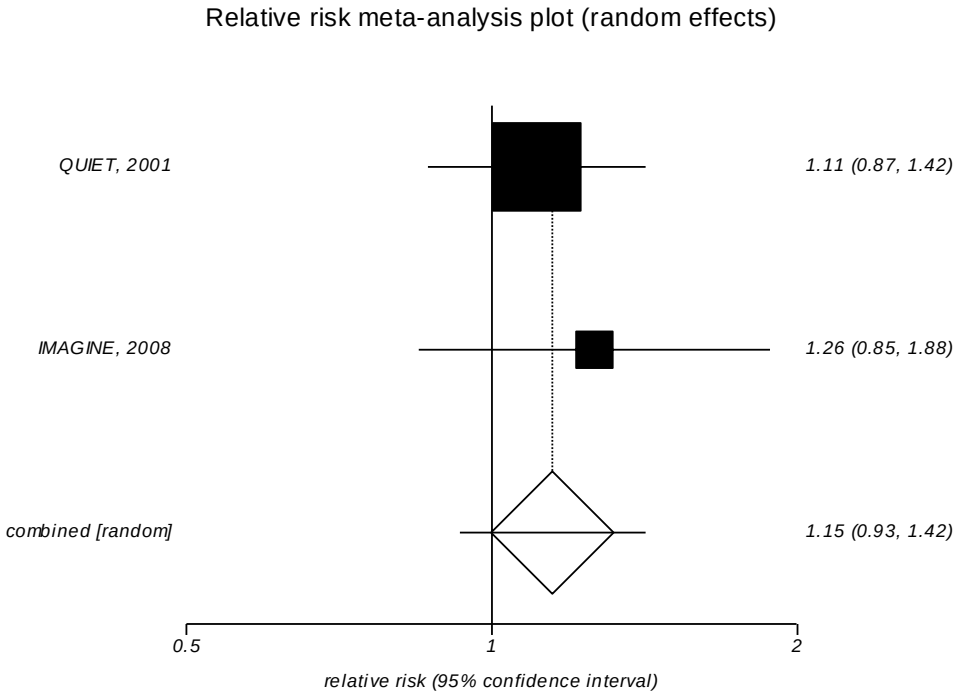


Test for heterogeneity: Cochran Q=4.040768 (df=3) p=0.2571
I^2 statistic=25.8%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 41. KQ3 Revascularizations Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease who have recently undergone, or are set to undergo, coronary artery bypass grafting surgery only



Test for heterogeneity: Cochran Q=0.291311 (df=1) p=0.5894
I^2 statistic=N/A

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 21. KQ4 Run-in Phase Data - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Run-in	Description	Exclusions
HOPE, 2000[38]	Yes	Ramipril 2.5mg/d X 7-10d, then placebo qd X 10-14d	1,035/10,576 (9.8%) excluded: - Non-compliance (n=NR) - ADE (n=NR) - Abnormal Scr or potassium (n=NR) - Withdrawal of consent (n=NR)
PART-2, 2000[41]	Yes	Ramipril 5mg/d X 7d, then 10mg/d X 7d	127/744 (17%) excluded: - Ineligibility (n=52, 41%) - Suspected ADE (n=52, 41%) - Patient preference (n=23, 18%)
SCAT, 2000[42]	Yes	Dietary and SB placebo X 1 month	~33% excluded†
EUROPA, 2003[43]	Yes	Perindopril 4mg/d X14d, then 8mg/d X 14d‡	1,437/13,655 (10.5%) excluded: - Hypotension (n=290, 20.2%) - Raised Scr or potassium (n=149, 10.4%) - Other intolerance (n=332, 23.1%) - Major clinical event (n=75, 5.2%) - Poor adherence (n=80, 5.6%) - Exclusion criteria (n=44, 3.1%) - Withdrawn consent (n=9, 0.6%) - Unspecified stop reason (n=446, 31%) - Never randomized (n=12, 0.8%)
Kondo et al, 2003[44]	No	N/A	N/A
CAMELOT, 2004[45]	Yes	Placebo tablet + placebo capsule qd X 14d	NR
JMIC-B, 2004[46]	No	N/A	N/A
PEACE, 2004[47]	Yes	Trandolapril 2mg/d X 14d	NR
FOSIDIAL, 2006[48]	Yes	Single-blind placebo X 14d, then fosinopril 5mg X1 dose	NR
Takahashi et al, 2006[49]	No	N/A	N/A
SMILE-ISCHEMIA, 2007[50]	No	N/A	N/A

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 21 Continued. KQ4 Run-in Phase Data - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease.

Study, year	Run-in	Description	Exclusions
TRANSCEND, 2008[51]	Yes	Placebo qd X 7d, then Telmisartan 80mg/d X 14d	740/6666 (11.1%) excluded: - Poor compliance (n=311, 42.0%) - Consent withdrawn (n=135, 18.2%) - Raised Scr or potassium (n=37, 5.0%) - Symptomatic hypotension (n=53, 7.2%) - Deaths (n=3, 0.4%) - Other reasons (n=201, 27.2%)

† = Specific numbers of patients who entered run-in, and number who were excluded following run-in were not provided
‡ = Patients >70 years old received Perindopril 2mg/d X 7d, then 4mg/d X 7d, then 8mg/d X 14d during run-in period

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 22. KQ4 Study Withdrawals - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease.

Study, year	Report Withdrawals	Group	n	Reasons
HOPE, 2000[38]	Yes	Ramipril	1511 (32.5%)	Cough (n=340, 7.3%) Hypotension/Dizziness (n=88, 1.9%) Angioedema (n=17, 0.4%) Uncontrolled HTN (n=109, 2.3%) Clinical Events (n=309, 6.7%) Other (n=1101, 23.7%)
		Placebo	1430 (30.7%)	Cough (n=85, 1.8%) Hypotension/Dizziness (n=70, 1.5%) Angioedema (n=7, 0.2%) Uncontrolled HTN (n=183, 3.9%) Clinical Events (n=418, 9.0%) Other (n=1074, 23.1%)
PART-2, 2000[41]	Yes	Ramipril	53 (17.2%)	Suspected ADE (n=31, 10%) Patient preference (n=22, 7%)
		Placebo	25 (8.1%)	Suspected ADE (n=3, 1%) Patient preference (n=22, 7%)
SCAT, 2000[42]	No	Enalapril	N/A	N/A
		Placebo		

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 22 Continued. KQ4 Study Withdrawals - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease.

Study, year	Report Withdrawals	Group	n	Reasons
EUROPA, 2003[43]	Yes	Perindopril	1391 (22.8%)	Cough (n=162, 2.7%) Hypotension (n=60, 1.0%) Kidney failure (n=20, 0.3%) Intolerance (n=144, 2.4%) Study endpoint (n=376, 6.2%) Hypertension (n=22, 0.4%) Refusal to continue (n=261, 4.3%) Other (n=347, 5.7%)
		Placebo	1266 (20.7%)	Cough (n=32, 0.5%) Hypotension (n=17, 0.3%) Kidney failure (n=16, 0.3%) Intolerance (n=80, 1.3%) Study endpoint (n=460, 7.5%) Hypertension (n=46, 0.8%) Refusal to continue (n=257, 4.2%) Other (n=359, 5.9%)
Kondo et al, 2003[44]	Yes	Candesartan	9 (4.4%)	Dizziness/Lightheadedness (n=9, 4.4%)
		Control	2 (1.0%)	Relocation (n=2, 1.0%)

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 22 Continued. KQ4 Study Withdrawals - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease.

Study, year	Report Withdrawals	Group	n	Reasons
CAMELOT, 2004[45]	Yes	Enalapril	236 (35.0%)	ADE (n=102, 15.1%) Withdrew consent (n=33, 4.9%) Death (n=4, 0.6%) Protocol violation (n=6, 0.9%) Laboratory abnormality (n=3, 0.4%) Lost to follow-up (n=22, 3.3%) Insufficient response (n=5, 0.7%) Other (n=61, 9.0%)
		Amlodipine	194 (29.2%)	ADE (n=87, 13.1%) Withdrew consent (n=38, 5.7%) Death (n=2, 0.3%) Laboratory abnormality (n=2, 0.3%) Lost to follow-up (n=18, 2.7%) Insufficient response (n=2, 0.3%) Other (n=45, 6.8%)
		Placebo	204 (31.1%)	ADE (n=71, 10.8%) Withdrew consent (n=50, 7.6%) Death (n=5, 0.8%) Protocol violation (n=8, 1.2%) Laboratory abnormality (n=3, 0.5%) Lost to follow-up (n=16, 2.4%) Insufficient response (n=3, 0.5%) Other (n=48, 7.3%)

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 22 Continued. KQ4 Study Withdrawals - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease.

Study, year	Report Withdrawals	Group	n	Reasons
JMIC-B, 2004[46]	Yes	ACEI∝	143 (17.4%)	ADE (n=72, 8.8%) No effect (n=20, 2.4%) Withdrawal of consent (n=10, 1.2%) Protocol deviation (n=5, 0.6%) Alleviating symptoms (n=11, 1.3%) Others (n=25, 3.0%)
		Nifedipine	107 (12.9%)	ADE (n=41, 5.0%) No effect (n=11, 1.3%) Withdrawal of consent (n=9, 1.1%) Protocol deviation (n=9, 1.1%) Alleviating symptoms (n=17, 2.1%) Others (n=20, 2.4%)
PEACE, 2004†[47]	No	Trandolapril	N/A	N/A
		Placebo		
FOSIDIAL, 2006[48]	Yes	Fosinopril	7 (3.6%)	Renal transplantation (n=7, 3.6%)
		Placebo	10 (5.0%)	Renal transplantation (n=8, 4.0%) Protocol violations (n=2, 1.0%)
Takahashi et al, 2006[49]	Yes	Candesartan	0 (0%)	N/A
		Control	0 (0%)	
SMILE-ISCHEMIA, 2007[50]	Yes	Zofenopril	46 (13.2%)	Major protocol violation (n=15, 4.3%) Lost to follow-up (n=3, 0.9%) Inability to perform treadmill test (n=31, 8.9%)
		Placebo		

∝ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril
† = Listed as side effects leading to discontinuation of the study medication

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 22 Continued. KQ4 Study Withdrawals - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease.

Study, year	Report Withdrawals	Group	n	Reasons
TRANSCEND, 2008[51]	Yes	Telmisartan	1090 (36.9%)	Hypotensive symptoms (n=29, 1.0%) Syncope (n=1, 0.03%) Cough (n=15, 0.5%) Diarrhea (n=7, 0.2%) Angioedema (n=2, 0.07%) Renal abnormalities (n=24, 0.8%)
		Placebo	1143 (38.5%)	Hypotensive symptoms (n=16, 0.5%) Syncope (n=0, 0%) Cough (n=18, 0.6%) Diarrhea (n=2, 0.07%) Angioedema (n=3, 0.1%) Renal abnormalities (n=13, 0.4%)

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 23. KQ4 Withdrawals Due To Adverse Events - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 Risk Factor	NR	Ramipril Placebo	NR	NR
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	Suspected adverse drug reactions leading to stopping randomized treatment	Ramipril Placebo	31/308 3/309	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Discontinuations due to adverse events	Enalapril Amlodipine Placebo	102/673 87/663 71/655	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	Withdrawals due to adverse events	ACEI$^{\propto}$ Nifedipine	72/822 41/828	NR
PEACE, 2004[47]	RCT	Documented CAD	Side effects leading to discontinuation of study medication	Trandolapril Placebo	599/4158 269/4132	NR
FOSIDIAL, 2006[48]	RCT	Hemodialysis and LVH	NR	Fosinopril Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril Placebo	NR	NR

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 23 Continued. KQ4 Withdrawals Due To Adverse Events - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease.

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	NR	Telmisartan Placebo	NR	NR

∝ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 24. KQ4 Hypotension - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38†]	RCT	CAD, Stroke, PVD or DM + 1 Risk Factor	Hypotension	Ramipril Placebo	2/4645 3/4652	NR
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	NR	Ramipril Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Hypotension	Enalapril Amlodipine Placebo	64/673 22/663 21/655	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI∝ Nifedipine	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	NR	Trandolapril Placebo	NR	NR
FOSIDIAL, 2006[48]	RCT	Hemodialysis and LVH	NR	Fosinopril Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	Severe hypotension	Zofenopril Placebo	2/172 2/177	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	NR	Telmisartan Placebo	NR	NR

† = Data are reported as "serious adverse events" found within the New Drug Application from www.fda.gov.

∝ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 25. KQ4 Syncope - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38†]	RCT	CAD, Stroke, PVD or DM + 1 Risk Factor	Syncope	Ramipril Placebo	3/4645 1/4652	NR
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	NR	Ramipril Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	NR	Enalapril Amlodipine Placebo	NR	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI∝ Nifedipine	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	Syncope	Trandolapril Placebo	200/4158 161/4132	NR
FOSIDIAL, 2006[48]	RCT	Hemodialysis and LVH	NR	Fosinopril Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	NR	Telmisartan Placebo	NR	NR

† = Data are reported as "serious adverse events" found within the New Drug Application from www.fda.gov.

∝ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 26. KQ4 Cough - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38†]	RCT	CAD, Stroke, PVD or DM + 1 Risk Factor	Cough	Ramipril Placebo	16/4645 9/4652	NR
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	NR	Ramipril Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	Cough	Enalapril Amlodipine Placebo	84/673 34/663 38/655	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI$^{\propto}$ Nifedipine	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	Cough	Trandolapril Placebo	1626/4158 1136/4132	NR
FOSIDIAL, 2006[48]	RCT	Hemodialysis and LVH	NR	Fosinopril Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	NR	Telmisartan Placebo	NR	NR

$\propto$ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril

† = Data are reported as "serious adverse events" found within the New Drug Application from www.fda.gov.

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 27. KQ4 Angioedema - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38†]	RCT	CAD, Stroke, PVD or DM + 1 Risk Factor	Angioedema	Ramipril Placebo	5/4645 1/4652	NR
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	NR	Ramipril Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	NR	Enalapril Amlodipine Placebo	NR	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI$^{\propto}$ Nifedipine	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	Angioedema	Trandolapril Placebo	8/4158 5/4132	NR
FOSIDIAL, 2006[48]	RCT	Hemodialysis and LVH	NR	Fosinopril Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	NR	Telmisartan Placebo	NR	NR

† = Data are reported as "serious adverse events" found within the New Drug Application from www.fda.gov.

$\propto$ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 28. KQ4 Hyperkalemia - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2005[38†]	RCT	CAD, Stroke, PVD or DM + 1 Risk Factor	Serum potassium level > 5.0 mmol/L	Ramipril Placebo	395/4539 297/4572	NR
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	NR	Ramipril Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	NR	Enalapril Amlodipine Placebo	NR	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI$^{\propto}$ Nifedipine	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	NR	Trandolapril Placebo	NR	NR
FOSIDIAL, 2006[48]	RCT	Hemodialysis and LVH	NR	Fosinopril Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	Serum potassium level > 5.5 mmol/L	Telmisartan Placebo	111/2954 49/2972	NR

† = Data taken from Mann JFE, et al. Serum potassium, cardiovascular risk, and effects of an ACE inhibitor: results of the HOPE Study. Clin Nephrol 2005;63:181-7; $\propto$ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 29. KQ4 Blood Dyscrasias - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 Risk Factor	NR	Ramipril Placebo	NR	NR
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	NR	Ramipril Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	NR	Enalapril Amlodipine Placebo	NR	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI$^{\propto}$ Nifedipine	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	NR	Trandolapril Placebo	NR	NR
FOSIDIAL, 2006[48]	RCT	Hemodialysis and LVH	NR	Fosinopril Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	NR	Telmisartan Placebo	NR	NR

$\propto$ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril

Appendix C: Additional Evidence Tables and Analyses

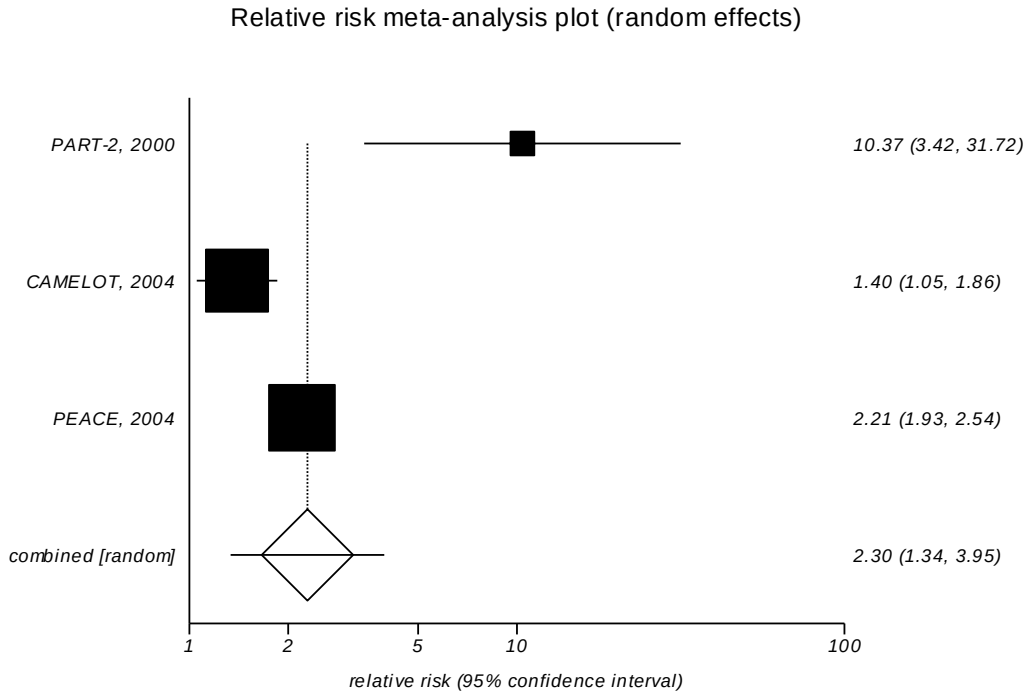
Appendix Table 30. KQ4 Rash - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
HOPE, 2000[38]	RCT	CAD, Stroke, PVD or DM + 1 Risk Factor	NR	Ramipril Placebo	NR	NR
PART-2, 2000[41]	RCT	MI, angina with confirmed CAD, TIA or IC	NR	Ramipril Placebo	NR	NR
SCAT, 2000[42]	RCT	Coronary atherosclerosis in >3 major arteries, elevated cholesterol	NR	Enalapril Placebo	NR	NR
EUROPA, 2003[43]	RCT	CAD (previous MI, revasc. or >70% coronary artery narrowing) without HF	NR	Perindopril Placebo	NR	NR
Kondo et al, 2003[44]	RCT	H/o coronary intervention with no significant stenosis on 6 mo f/o angiography	NR	Candesartan Control	NR	NR
CAMELOT, 2004[45]	RCT	PCI or chest pain requiring coronary angiography	NR	Enalapril Amlodipine Placebo	NR	NR
JMIC-B, 2004[46]	RCT	Hypertension and CAD	NR	ACEI$^{\propto}$ Nifedipine	NR	NR
PEACE, 2004[47]	RCT	Documented CAD	NR	Trandolapril Placebo	NR	NR
FOSIDIAL, 2006[48]	RCT	Hemodialysis and LVH	NR	Fosinopril Placebo	NR	NR
Takahashi et al, 2006[49]	RCT	Chronic maintenance hemodialysis	NR	Candesartan Control	NR	NR
SMILE-ISCHEMIA, 2007[50]	RCT	MI within 6 weeks	NR	Zofenopril Placebo	NR	NR
TRANSCEND, 2008[51]	RCT	CAD, Cerebrovascular disease, PVD, or DM + end-organ damage	NR	Telmisartan Placebo	NR	NR

$\propto$ = Patients in the ACEI group were given enalapril, imidapril, or lisinopril

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 42. KQ4 Withdrawal Due To Adverse Events Subgroup ACEI Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease



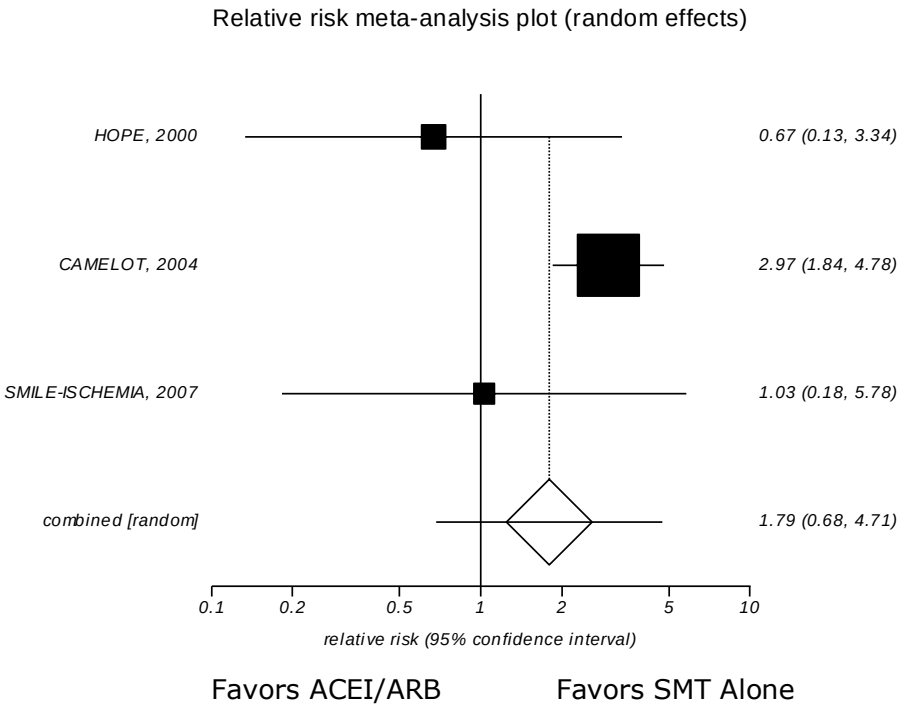
Favors ACEI Favors SMT Alone

Test for heterogeneity: Cochran Q=15.650446 (df=2) p=0.0004
I^2 statistic=87.2%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 43. KQ4 Hypotension ACEI Subgroup Analysis - Meta-analysis of randomized placebo-controlled trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=3.368646 (df=2) p=0.1856
I^2 statistic=40.6%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 31. KQ6 Run-in Phase Date - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Run-in	Description	Exclusions
MARCATOR, 1995[53]	No	N/A	N/A
APRES, 2000[54]	No	N/A	N/A
Kondo et al, 2001[55]	No	N/A	N/A
PARIS, 2001[56]	No	N/A	N/A
QUIET, 2001[57]	No	N/A	N/A
AACHEN, 2006[58]	No	N/A	N/A
IMAGINE, 2008[59]	No	N/A	N/A

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 32. KQ6 Study Withdrawals - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Report Withdrawals	Group	n	Reasons
MARCATOR, 1995[53]	Yes	Cilazapril Placebo	350 (24.4%)†	No follow-up angiogram (n=159, 11.1%) Protocol violation (n=22, 1.5%) Severe hypotension (n=33, 2.3%) Severe cough (n=21, 1.5%) Angina pectoris (range 10-14% per group)
APRES, 2000[54]	Yes	Ramipril Placebo	13 (16.3%) 13 (16.5%)	Open-label ACEI treatment (n=5, 6.3%) Loss of consent/follow-up (n=5, 6.3%) Side effects (n=2, 2.5%) Endocarditis requiring surgery (n=1, 1.3%) Open-label ACEI treatment (n=7, 8.9%) Loss of consent/follow-up (n=4, 5.1%) Side effects (n=2, 2.5%)
Kondo, 2001[55]	Yes	Quinapril Control	1 (2%) 0 (0%)	Severe cough (n=1, 2%) N/A
PARIS, 2001[56]	Yes	Quinapril Placebo	0 (0%) 0 (0%)	N/A 0 (0%)
QUIET, 2001[57]	Yes	Quinapril Placebo	246 (28.0%) 218 (25.0%)	NR NR
AACHEN, 2006[58]	No	Candesartan Placebo	N/A	N/A
IMAGINE, 2008[59]	Yes	Quinapril Placebo	444 (34.7%) 321 (25.2%)	Adverse event (n=228, 17.8%) Worsening diabetes (n=8, 0.6%) Patient decision (n=103, 8.0%) Physician decision (n=73, 5.7%) Other (n=32, 2.5%) Adverse event (n=103, 8.1%) Worsening diabetes (n=3, 0.2%) Patient decision (n=89, 7.0%) Physician decision (n=97, 7.6%) Other (n=23, 1.8%)

† = Reasons for all 350 patient withdrawals was not given

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 33. KQ6 Withdrawals Due To Adverse Events - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%)(5-7 days prior to randomization) or PTCA (18%)(1-2 days prior to randomization) for angina	Withdrawal due to side effects	Ramipril Placebo	2/80 2/79	NR
Kondo, 2001[55]	RCT	Received elective balloon angioplasty followed by coronary stenting	Dropped out of the study due to adverse events	Quinapril Control	1/49 0/50	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	N/A†	Quinapril Placebo	0/46 0/45	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Discontinuations due to adverse events	Quinapril Placebo	228/1280 103/1273	NR

† All patients were followed-up

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 34. KQ6 Hypotension - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%)(5-7 days prior to randomization) or PTCA (18%)(1-2 days prior to randomization) for angina	NR	Ramipril Placebo	NR	NR
Kondo, 2001[55]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Hypotension	Quinapril Placebo	154/1280 70/1273	Absolute difference 6.5% (4.5% to 8.5%)

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 35. KQ6 Syncope - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%)(5-7 days prior to randomization) or PTCA (18%)(1-2 days prior to randomization) for angina	NR	Ramipril Placebo	NR	NR
Kondo, 2001[55]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	NR	Quinapril Placebo	NR	NR

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 36. KQ6 Cough - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%)(5-7 days prior to randomization) or PTCA (18%)(1-2 days prior to randomization) for angina	NR	Ramipril Placebo	NR	NR
Kondo, 2001[55]	RCT	Received elective balloon angioplasty followed by coronary stenting	Severe cough	Quinapril Control	1/49 0/50	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	Cough	Quinapril Placebo	33/878 2/872	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	Cough	Quinapril Placebo	269/1280 141/1273	Absolute difference 10% (7.2% to 12.7%)

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 37. KQ6 Angioedema - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%)(5-7 days prior to randomization) or PTCA (18%)(1-2 days prior to randomization) for angina	NR	Ramipril Placebo	NR	NR
Kondo, 2001[55]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	NR	Quinapril Placebo	NR	NR

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 38. KQ6 Hyperkalemia - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%)(5-7 days prior to randomization) or PTCA (18%)(1-2 days prior to randomization) for angina	Electrolytic derangement	Ramipril Placebo	0/80 0/79	NR
Kondo, 2001[55]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	NR	Quinapril Placebo	NR	NR

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 39. KQ6 Rash - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%)(5-7 days prior to randomization) or PTCA (18%)(1-2 days prior to randomization) for angina	NR	Ramipril Placebo	NR	NR
Kondo, 2001[55]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	NR	Quinapril Placebo	NR	NR

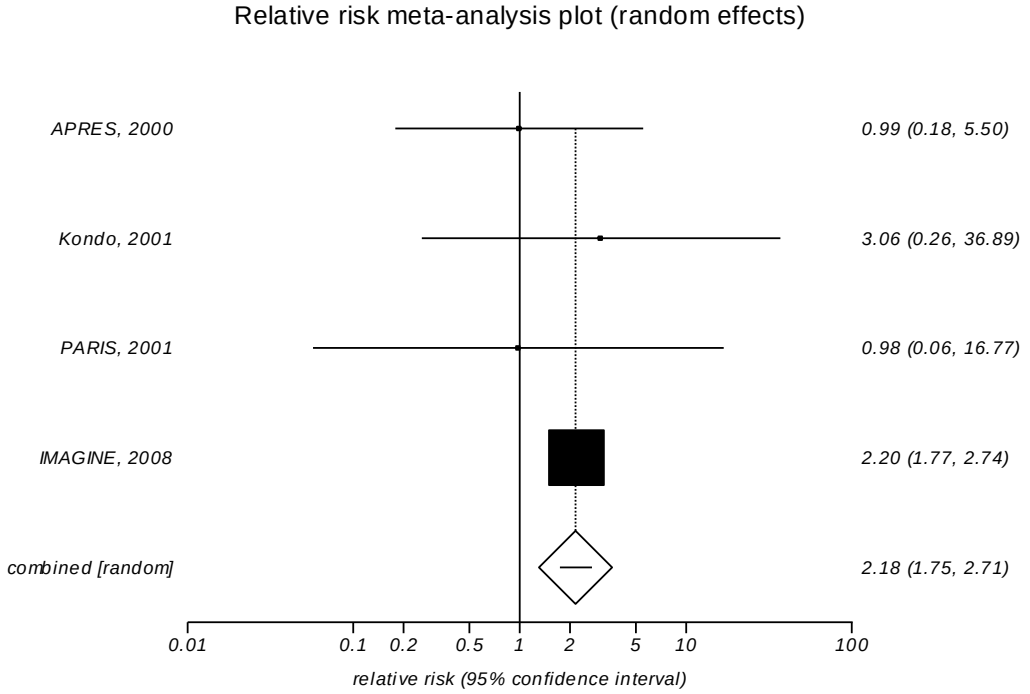
Appendix C: Additional Evidence Tables and Analyses

Appendix Table 40. KQ6 Blood Dyscrasias - Comparative effectiveness of medical therapies with or without ACEI or ARBs for stable ischemic heart disease

Study, year	Study Design	Population	Outcome/Definition	Group	Events, n/N	Events, "X"R (95% CI)
MARCATOR, 1995[53]	RCT	Undergoing elective coronary angioplasty	NR	Cilazapril Placebo	NR	NR
APRES, 2000[54]	RCT	Underwent elective CABG (82%)(5-7 days prior to randomization) or PTCA (18%)(1-2 days prior to randomization) for angina	NR	Ramipril Placebo	NR	NR
Kondo, 2001[55]	RCT	Received elective balloon angioplasty followed by coronary stenting	NR	Quinapril Control	NR	NR
PARIS, 2001[56]	RCT	Underwent successful elective PCI with stent implantation	NR	Quinapril Placebo	NR	NR
QUIET, 2001[57]	RCT	Underwent successful elective coronary angioplasty of atherectomy within 12-72 hours	NR	Quinapril Placebo	NR	NR
AACHEN, 2006[58]	RCT	Undergoing elective coronary stent implantation (treatment started 7-14 days prior to intervention)	NR	Candesartan Placebo	NR	NR
IMAGINE, 2008[59]	RCT	Underwent CABG (7-10 days prior)	NR	Quinapril Placebo	NR	NR

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 44. KQ6. Withdrawals Due To Adverse Events Sensitivity Analysis - Meta-analysis of randomized placebo-controlled + open-label trials in patients with stable ischemic heart disease

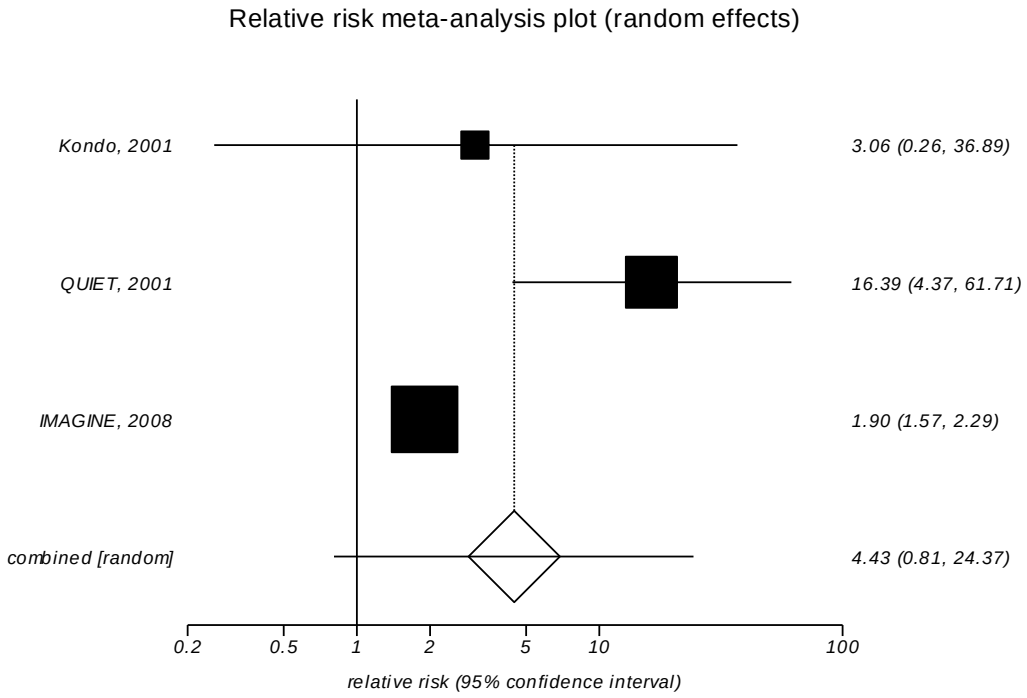


Test for heterogeneity: Cochran Q=0.856866 (df=3) p=0.8358
I^2 statistic=0%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Figure 45. KQ6. Cough Sensitivity Analysis - Meta-analysis of randomized placebo-controlled + open-label trials in patients with stable ischemic heart disease



Test for heterogeneity: Cochran Q=9.185671 (df=2) p=0.0101
I^2 statistic=78.2%

Note: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95% confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 41. KQ1 - Strength of Evidence Grading

Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control*	Relative Risk (95% CI)	Absolute Risk	Evidence Grade	Importance
Total mortality - IHD (follow-up 2-4.8 years)												
7	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	1552/19077 (8.1%)	1714/19059 (9%) 0.9% 12%	RR 0.91 (0.84 to 0.98)	8 fewer per 1000 (from 2 fewer to 14 fewer) 0 fewer per 1,000 10 fewer per 1,000	HIGH	CRITICAL
Total mortality - vs. CCB (follow-up 2-3 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	23/1495 (1.5%)	19/1491 (1.3%) 1.1% 1.4%	RR 1.21 (0.66 to 2.21)	3 more per 1000 (from 4 fewer to 16 more) 2 more per 1,000 2 more per 1,000	MODERATE	CRITICAL
Total mortality - IHD risk equivalents (follow-up 1.6-4.8 years)												
1	randomized trial	single trial	no serious inconsistency	no serious indirectness	very serious	none	53/196 (27.0%)	50/201 (24.9%)	RR 1.08 (0.78 to 1.52)	158 fewer per 1000 (from 234 fewer to 1000 more)	LOW	CRITICAL
Cardiovascular mortality - IHD (follow-up 2-4.8 years)												
6	randomized trial	no serious limitations	serious	no serious indirectness	serious	none	883/18848 (4.7%)	1021/18828 (5.4%) 0.3% 8.1%	RR 0.87 (0.75 to 1.02)	7 fewer per 1000 (from 14 fewer to 1 more) 0 fewer per 1,000 10 fewer per 1,000	LOW	CRITICAL
Cardiovascular mortality - vs. CCB (follow-up 2-3 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	11/1495 (0.7%)	11/1491 (0.7%) 0.73% 0.75%	RR 1.00 (0.43 to 2.29)	0 fewer per 1000 (from 4 fewer to 9 more) 0 fewer per 1,000 0 fewer per 1,000	MODERATE	CRITICAL

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Cardiovascular mortality - IHD risk equivalents (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	32/196 (16.3%)	31/201 (15.4%)	RR 1.06 (0.67 to 1.67)	9 more per 1000 (from 51 fewer to 103 more)	MODERATE	CRITICAL
Nonfatal myocardial infarction - IHD (follow-up 2-4.8 years)												
6	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	813/16123 (5%)	981/16087 (6.1%) 2.9% 7.2%	RR 0.83 (0.73 to 0.94)	10 fewer per 1000 (from 4 fewer to 16 fewer) 4 fewer per 1,000 12 fewer per 1,000	HIGH	CRITICAL
Nonfatal myocardial infarction - vs. CCB (follow-up 2 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	11/673 (1.6%)	14/663 (2.1%)	RR 0.77 (0.35 to 1.69)	5 fewer per 1000 (from 14 fewer to 14 more)	MODERATE	CRITICAL
Nonfatal myocardial infarction - IHD risk equivalents (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	very serious	none	9/196 (4.6%)	7/201 (3.5%)	RR 1.31 (0.50 to 3.47)	11 more per 1000 (from 18 fewer to 86 more)	LOW	CRITICAL
Stroke - IHD (follow-up 2-4.8 years)												
7	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	454/19077 (2.4%)	581/19059 (3%) 1.3% 4.9%	RR 0.79 (0.67 to 0.93)	6 fewer per 1000 (from 2 fewer to 10 fewer) 2 fewer per 1,000 10 fewer per 1,000	HIGH	CRITICAL
Stroke - vs. CCB (follow-up 2-3 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	24/1495 (1.6%)	22/1491 (1.5%) 0.9% 1.9%	RR 1.09 (0.61 to 1.94)	1 more per 1000 (from 6 fewer to 14 more) 0 more per 1,000 1 more per 1,000	MODERATE	CRITICAL
Stroke - IHD risk equivalents (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	very serious	none	18/196 (9.2%)	11/201 (5.5%)	RR 1.60 (0.81 to 3.46)	33 more per 1000 (from 10 fewer to 135 more)	LOW	CRITICAL
Cardiovascular mortality, myocardial infarction, stroke - IHD (follow-up 4.5-4.8 years)												
3	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	1431/11757 (12.2%)	1686/11756 (14.3%) 10%	RR 0.86 (0.77 to 0.95)	20 fewer per 1000 (from 7 fewer to 33 fewer) 13 fewer per 1,000	HIGH	CRITICAL

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								18%		25 fewer per 1,000		
Cardiovascular mortality, myocardial infarction, stroke - IHD risk equivalents (follow-up 4.8 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	very serious	none	48/196 (24.5%)	41/201 (20.4%)	RR 1.20 (0.83 to 1.73)	41 more per 1000 (from 35 fewer to 149 more)	MODERATE	CRITICAL
Atrial fibrillation - IHD (follow-up 4.5-4.7 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	268/7245 (3.7%)	271/7016 (3.9%)	RR 0.98 (0.83 to 1.15)	1 fewer per 1000 (from 7 fewer to 6 more)	HIGH	IMPORTANT
								2.3%		0 fewer per 1,000		
								6.1%		1 fewer per 1,000		
Angina symptoms: Treadmill exercise test (follow-up 6 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	151	152	WMD 3.5 minutes	3.5 (2.82 to 4.18)	MODERATE	IMPORTANT
Total Hospitalizations – IHD (follow-up 4.7 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	1756/3262 (53.8%)	1815/3281 (55.3%)	RR 0.97 (0.94 to 1.00)	17 fewer per 1000 (from 33 fewer to 0 more)	MODERATE	IMPORTANT
								51%		15 fewer per 1,000		
								94%		28 fewer per 1,000		
Hospitalizations for angina - IHD (follow-up 2-4.7 years)												
5	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	978/8809 (11.1%)	1007/8819 (11.4%)	RR 0.97 (0.89 to 1.06)	3 fewer per 1000 (from 13 fewer to 7 more)	HIGH	IMPORTANT
								9.7%		2 fewer per 1,000		
								13.6%		4 fewer per 1,000		
Hospitalizations for angina - vs. CCB (follow-up 2-3 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	142/1498 (9.5%)	101/1491 (6.8%)	RR 1.38 (0.95 to 2.02)	26 more per 1000 (from 3 fewer to 69 more)	MODERATE	IMPORTANT
								6%		22 more per 1,000		
								7.7%		29 more per 1,000		
Hospitalizations for heart failure - IHD (follow-up 2-4.8 years)												
6	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	454/18848 (2.4%)	540/18828 (2.9%)	RR 0.83 (0.70 to 0.98)	5 fewer per 1000 (from 1 fewer to 9 fewer)	HIGH	IMPORTANT
								0.8%		1 fewer per 1,000		
								4.3%		7 fewer per 1,000		
Hospitalizations for heart failure - vs. CCB (follow-up 2-3 years)												

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2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	13/1495 (0.9%)	15/1491 (1%) 0.5% 1.4%	RR 0.87 (0.41 to 1.83)	1 fewer per 1000 (from 6 fewer to 8 more) 0 fewer per 1,000 1 fewer per 1,000	MODERATE	IMPORTANT
Need for revascularization - IHD (follow-up 2-4.7 years)												
5	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	1779/14611 (12.2%)	1971/14618 (13.5%) 9.8% 18.3%	RR 0.90 (0.85 to 0.96)	14 fewer per 1000 (from 5 fewer to 20 fewer) 9 fewer per 1,000 18 fewer per 1,000	HIGH	CRITICAL
Need for revascularization - vs. CCB (follow-up 2-3 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	170/1495 (11.4%)	159/1491 (10.7%) 9.8% 11.8%	RR 1.06 (0.83 to 1.36)	6 more per 1000 (from 18 fewer to 39 more) 5 more per 1,000 7 more per 1,000	MODERATE	CRITICAL

*Risk in the control group is reported as observed pooled, low and high-risks derived from included trials

Abbreviations: CCB=calcium channel blocker; CI=confidence interval; CV=cardiovascular; IHD=ischemic heart disease; MI=myocardial infarction; RR=relative risk

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Appendix Table 42. KQ2 - Strength of Evidence Grading

Quality assessment							Summary of findings					
							No of patients		Effect		Evidence Grade	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control	Relative Risk (95% CI)	Absolute Risk		
Total mortality (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	1065/8502 (12.5%)	1014/8576 (11.8%)	RR 1.07 (0.98 to 1.16)	8 more per 1000 (from 2 fewer to 19 more)	MODERATE	CRITICAL
Cardiovascular mortality (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	620/8502 (7.3%)	603/8576 (7%)	RR 1.04 (0.93 to 1.17)	3 more per 1000 (from 5 fewer to 12 more)	MODERATE	CRITICAL
Mmyocardial infarction (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	438/8502 (5.2%)	413/8576 (4.8%)	RR 1.08 (0.94 to 1.23)	4 more per 1000 (from 3 fewer to 11 more)	MODERATE	CRITICAL
Stroke (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	373/8502 (4.4%)	405/8576 (4.7%)	RR 0.93 (0.81 to 1.07)	3 fewer per 1000 (from 9 fewer to 3 more)	MODERATE	CRITICAL
Cardiovascular mortality, myocardial infarction, stroke (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	no serious imprecision	none	1200/8502 (14.1%)	1210/8576 (14.1%)	RR 1.00 (0.93 to 1.09)	0 fewer per 1000 (from 10 fewer to 13 more)	HIGH	CRITICAL
New onset atrial fibrillation (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	537/8502 (6.3%)	570/8576 (6.6%)	RR 0.96 (0.85 to 1.07)	3 fewer per 1000 (from 10 fewer to 5 more)	MODERATE	IMPORTANT
Worsening/new angina (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	538/8502 (6.3%)	567/8576 (6.6%)	RR 0.96 (0.85 to 1.08)	3 fewer per 1000 (from 10 fewer to 5 more)	MODERATE	IMPORTANT
Hospitalization for angina (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	952/8502 (11.2%)	925/8576 (10.8%)	RR 1.04 (0.95 to 1.14)	4 more per 1000 (from 5 fewer to 15 more)	MODERATE	IMPORTANT
Hospitalization for heart failure (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	serious	none	332/8502 (3.9%)	354/8576 (4.1%)	RR 0.95 (0.82 to 1.1)	2 fewer per 1000 (from 7 fewer to 4 more)	MODERATE	CRITICAL

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Revascularization (follow-up 56 months)												
1	randomized trial	no serious limitations	single study	no serious indirectness	no serious imprecision	none	1303/8502 (15.3%)	1269/8576 (14.8%)	RR 1.04 (0.97 to 1.13)	6 more per 1000 (from 4 fewer to 19 more)	Moderate	CRITICAL

Abbreviations: CI=confidence interval; RR=relative risk

Appendix C: Additional Evidence Tables and Analyses

Appendix Table 43. KQ3 - Strength of Evidence Grading

Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control*	Relative Risk (95% CI)	Absolute Risk	Evidence Grade	Importance
Total mortality (follow-up 0.5-3 years)												
6	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	64/3422 (1.9%)	64/2687 (2.4%)	RR 0.94 (0.67 to 1.37)	1 fewer per 1000 (from 8 fewer to 9 more)	MODERATE	CRITICAL
								0%		0 fewer per 1,000		
								10%		6 fewer per 1,000		
Cardiovascular mortality (follow-up 0.5-3 years)												
5	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	32/2347 (1.4%)	37/2326 (1.6%)	RR 0.91 (0.53 to 1.57)	1 fewer per 1000 (from 8 fewer to 9 more)	MODERATE	CRITICAL
								0%		0 fewer per 1,000		
								10%		8 fewer per 1,000		
Nonfatal myocardial infarction (follow-up 0.5-3 years)												
5	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	81/3342 (2.4%)	71/2608 (2.7%)	RR 0.89 (0.65 to 1.24)	3 fewer per 1000 (from 9 fewer to 6 more)	MODERATE	CRITICAL
								0%		0 fewer per 1,000		
								4.6%		5 fewer per 1,000		
Stroke (follow-up 2.8-3 years)												
2	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	15/1360 (1.1%)	15/1352 (1.1%)	RR 1.01 (0.50 to 2.04)	0 fewer per 1000 (from -1 fewer to 1 more)	MODERATE	CRITICAL
								1.1%		0 more per 1,000		
								1.3%		0 more per 1,000		
Cardiovascular mortality, myocardial infarction, stroke (follow-up 3 years)												
1	randomized trial	no serious limitations	single trial	no serious indirectness	serious	none	45/1280 (3.5%)	45/1273 (3.5%)	RR 0.99 (0.66 to 1.49)	0 fewer per 1000 (from 12 fewer to 17 more)	MODERATE	CRITICAL
Atrial fibrillation (follow-up 3 years)												
1	randomized trial	no serious limitations	single trial	no serious indirectness	serious	none	114/1280 (8.9%)	101/1273 (7.9%)	RR 1.12 (0.87 to 1.45)	9 more per 1000 (from 10 fewer to 36 more)	MODERATE	IMPORTANT

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Hospitalization for angina (follow-up 2.3-3 years)												
3	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	102/2238 (4.6%)	99/2224 (4.5%) 3.0% 11.4%	RR 1.02 (0.78 to 1.34)	1 more per 1000 (from 10 fewer to 15 more) 0 more per 1,000 2 more per 1,000	HIGH	IMPORTANT
Hospitalization for heart failure (follow-up 3 years)												
1	randomized trial	no serious limitations	single trial	no serious indirectness	very serious	none	15/1280 (1.2%)	14/1273 (1.1%)	RR 1.07 (0.52 to 2.20)	1 more per 1000 (from 5 fewer to 13 more)	LOW	CRITICAL
Revascularization (follow-up 0.5-3 years)												
4	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	274/2464 (11.1%)	106/1736 (6.1%) 3.2% 15.6%	RR 1.28 (1.03 to 1.59)	17 more per 1000 (from 2 more to 36 more) 8 more per 1,000 43 more per 1,000	HIGH	CRITICAL

*Risk in the control group is reported as observed pooled, low and high-risks derived from included trials

Abbreviations: CI=confidence interval; RR=relative risk

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Appendix Table 44. KQ4 - Strength of Evidence Grading

Quality assessment							Summary of findings					
							No of patients		Effect		Evidence Grade	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Control		Relative (95% CI)	Absolute		
Withdrawals due to ADR - IHD (follow-up 2-4.8 years)												
3	randomised trial	no serious limitations	serious	no serious indirectness	serious	reporting bias	732/5139 (14.2%)	343/5096 (6.7%)	RR 2.30 (1.34 to 3.95)	87 more per 1000 (from 23 more to 198 more)	LOW	IMPORTANT
								1.0%		12 more per 1,000		
								10.8%		140 more per 1,000		
Withdrawals due to ADR - vs CCBs (follow-up 2-3 years)												
2	randomised trial	no serious limitations	serious	no serious indirectness	serious	reporting bias	174/1495 (11.6%)	128/1491 (8.6%)	RR 1.40 (0.92 to 2.12)	34 more per 1000 (from 7 fewer to 96 more)	LOW	IMPORTANT
								5.0%		19 more per 1,000		
								13.1%		52 more per 1,000		
Hypotension - IHD (follow-up 0.5-4.5 years)												
3	randomised trial	no serious limitations	serious	no serious indirectness	serious	reporting bias	68/5490 (1.2%)	26/5484 (0.5%)	RR 1.79 (0.68 to 4.71)	5 fewer per 1000 (from 5 fewer to 5 fewer)	LOW	IMPORTANT
								0.06%		0 fewer per 1,000		
								3.2%		32 fewer per 1,000		
Hypotension - vs CCBs (follow-up 2 years)												
1	randomised trial	no serious limitations	single trial	no serious indirectness	no serious imprecision	none	64/673 (9.5%)	22/663 (3.3%)	RR 2.87 (1.79 to 4.60)	62 more per 1000 (from 26 more to 119 more)	HIGH	IMPORTANT
Syncope - IHD (follow-up 4.5-4.8 years)												
2	randomised trial	no serious limitations	serious	no serious indirectness	serious	none	203/8803 (2.3%)	162/8784 (1.8%)	RR 1.24 (1.02 to 1.52)	4 more per 1000 (from 0 more to 9 more)	LOW	IMPORTANT
								0.2%		0 more per 1,000		
								3.9%		9 more per 1,000		
Cough - IHD (follow-up 2-4.8 years)												
3	randomised trial	no serious limitations	serious	no serious indirectness	serious	reporting bias	1729/9476 (18.2%)	1183/9439 (12.5%)	RR 1.67 (1.22 to 2.29)	84 more per 1000 (from 28 more to 161 more)	LOW	IMPORTANT
								0.2%		1 more per 1,000		
								27.5%		184 more per 1,000		
Cough - vs CCBs (follow-up 2 years)												
1	randomised trial	no serious limitations	single trial	no serious indirectness	no serious imprecision	none	84/673 (12.5%)	34/663 (5.1%)	RR 2.43 (1.66 to 3.57)	73 more per 1000 (from 34 more to 131 more)	HIGH	IMPORTANT
								0%		0 more per 1,000		

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Angioedema - IHD (follow-up 4.5-4.8 years)												
2	randomised trial	no serious limitations	serious	no serious indirectness	serious	none	13/8803 (0.1%)	6/8784 (0.1%) 0.2% 1.2%	RR 2.03 (0.75 to 5.47)	1 more per 1000 (from 0 fewer to 4 more) 2 more per 1,000 12 more per 1,000	LOW	IMPORTANT
Hyperkalemia - IHD (follow-up 4.5-4.7 years)												
2	randomised trial	no serious limitations	serious	no serious indirectness	serious	reporting bias	506/7493 (6.8%)	346/7544 (4.6%) 1.6% 6.5%	RR 1.71 (1.02 to 2.87)	33 more per 1000 (from 1 more to 86 more) 11 more per 1,000 46 more per 1,000	LOW	IMPORTANT

Abbreviations: CCB=calcium channel blocker; CI=confidence interval; CV=cardiovascular; IHD=ischemic heart disease; MI=myocardial infarction; RR=relative risk

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Appendix Table 45. KQ5 - Strength of Evidence Grading

Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control	Relative Risk (95% CI)	Absolute Risk	Evidence Grade	Importance
Study withdrawals (follow-up 56 months)												
1	randomized trial	no serious limitations	single trial	no serious indirectness	no serious imprecision	none	2495/8502 (29.3%)	2099/8576 (24.5%)	RR 1.20 (1.14 to 1.26)	49 more per 1000 (from 34 more to 64 more)	HIGH	IMPORTANT
Hypotension withdrawals (follow-up 56 months)												
1	randomized trial	no serious limitations	single trial	no serious indirectness	no serious imprecision	none	406/8502 (4.8%)	149/8576 (1.7%)	RR 2.75 (2.28 to 3.31)	30 more per 1000 (from 22 more to 39 more)	HIGH	IMPORTANT
Syncope withdrawals (follow-up 56 months)												
1	randomized trial	no serious limitations	single trial	no serious indirectness	serious	none	29/8502 (0.3%)	15/8576 (0.2%)	RR 1.95 (1.06 to 3.60)	2 more per 1000 (from 0 more to 5 more)	MODERATE	IMPORTANT
Cough withdrawals (follow-up 56 months)												
1	randomized trial	no serious limitations	single trial	no serious indirectness	no serious imprecision	none	392/8502 (4.6%)	360/8576 (4.2%)	RR 1.10 (0.96 to 1.26)	4 more per 1000 (from 2 fewer to 11 more)	HIGH	IMPORTANT
Angioedema withdrawals (follow-up 56 months)												
1	randomized trial	no serious limitations	single trial	no serious indirectness	very serious	none	18/8502 (0.2%)	25/8576 (0.3%)	RR 0.73 (0.40 to 1.32)	1 fewer per 1000 (from 2 fewer to 1 more)	LOW	IMPORTANT
Renal impairment withdrawals (follow-up 56 months)												
1	randomized trial	no serious limitations	single trial	no serious indirectness	no serious imprecision	none	94/8502 (1.1%)	60/8576 (0.7%)	RR 1.58 (1.15 to 2.18)	4 more per 1000 (from 1 more to 8 more)	HIGH	IMPORTANT

Abbreviations: CI=confidence interval; RR=relative risk

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Appendix Table 46. KQ6 - Strength of Evidence Grading

Quality assessment							Summary of findings					
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment	Control	Relative Risk (95% CI)	Absolute Risk	Evidence Grade	Importance
Study withdrawals (follow-up 0.5-3 years)												
3	randomized trial	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	230/1406 (16.4%)	105/1397 (7.5%)	RR 2.17 (1.75 to 2.7)	88 more per 1000 (from 56 more to 128 more)	HIGH	IMPORTANT
								0%		0 more per 1,000		
								8.1%		94 more per 1,000		
Hypotension (follow-up 3 years)												
1	randomized trial	no serious limitations	single study	no serious indirectness	no serious imprecision	none	154/120 (128.3%)	70/1273 (5.5%)	RR 2.19 (1.67 to 2.87)	65 more per 1000 (from 37 more to 103 more)	HIGH	IMPORTANT
Cough (follow-up 2.3-3 years)												
2	randomized trial	no serious limitations	serious	no serious indirectness	very serious	none	302/2158 (14%)	143/2145 (6.7%)	RR 4.97 (0.58 to 42.95)	266 more per 1000 (from 28 fewer to 1000 more)	LOW	IMPORTANT
								0.2%		7 more per 1,000		
								11.1%		440 more per 1,000		

*Risk in the control group is reported as observed pooled, low and high-risks derived from included trials

Abbreviations: CI=confidence interval; RR=relative risk

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Appendix Table 47. KQ7 - Strength of Evidence Grading

Quality assessment							Summary of findings		Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Findings	Evidence Grade	
Sex impact on benefits: ACE inhibitor vs. placebo									
2	randomized trial	serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the same in the two trials.	ACE inhibitors provide similar efficacy in males and females.	MODERATE	CRITICAL
Sex impact on benefits: ARB vs. placebo									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	ARBs may not reduce the composite endpoint in females as much as males.	LOW	CRITICAL
Sex impact on benefits: ACE inhibitor vs. ARB									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	ACE inhibitors may be superior to ARBs in females but similar in males.	LOW	CRITICAL
Sex impact on benefits: ACE inhibitor vs. ACE inhibitor + ARB									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	Combination therapy may be superior to ACE inhibitors in females but similar in males.	LOW	CRITICAL
Sex impact on benefits: ACE inhibitor vs. CCB									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	ACE inhibitors appear to be similar to CCBs in efficacy in either males or females.	LOW	CRITICAL

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Age impact on benefits: ACE inhibitor vs. placebo									
2	randomized trial	serious limitations	no serious imprecision	no serious indirectness	serious	Only the composite endpoint included in subgroup analyses. Composite endpoints not exactly the same in the two trials. Different age categories evaluated in different trials.	ACE inhibitors provide similar benefits in patients of different ages.	LOW	CRITICAL
Age impact on benefits: ARB vs. placebo									
1	randomized trial	serious limitations	single trial	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	ARBs provide similar benefits in patients of different ages.	LOW	CRITICAL
Age impact on benefits: ACE inhibitor vs. ARB									
1	randomized trial	serious limitations	single trial	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	ACE inhibitors provide similar benefits as ARBs in patients of different ages.	LOW	CRITICAL
Age impact on benefits: ACE inhibitor vs. ACE inhibitor + ARB									
1	randomized trial	serious limitations	single trial	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	ACE inhibitors provide similar benefits as combination therapy in patients of different ages.	LOW	CRITICAL
Age impact on benefits: ACE inhibitor vs. CCB									
1	randomized trial	serious limitations	single trial	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	ACE inhibitors provide similar benefits as calcium channel blockers in younger and older subjects.	LOW	CRITICAL
Diabetes mellitus impact on benefits: ACE inhibitor vs. Placebo									
2	randomized trial	serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses, which was not exactly the same in the two studies. Evaluated in subgroups (HOPE and EUROPA) and prespecified substudies (MICRO-HOPE, PERSUADE) from these trials.	ACE inhibitors provide similar benefits in those with and without diabetes mellitus.	MODERATE	CRITICAL

Appendix C: Additional Evidence Tables and Analyses

Diabetes mellitus impact on benefits: ARB vs. Placebo									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	ARBs provide similar benefits in those with and without diabetes mellitus.	LOW	CRITICAL
Diabetes mellitus impact on benefits: ACE inhibitor vs. ARB									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	ACE inhibitors provide similar benefits as ARBs in those with and without diabetes mellitus.	LOW	CRITICAL
Diabetes mellitus impact on benefits: ACE inhibitor vs. ACE inhibitor + ARB									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER.	Combination therapy may be better than ACE inhibitors alone amongst those with diabetes mellitus but similar in non-diabetics.	LOW	CRITICAL
Diabetes mellitus impact on benefits: ACE inhibitor vs. CCB									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses. Composite endpoint not exactly the one selected in the CER	ACE inhibitor therapy provides similar benefits as calcium channel blockers in subjects with diabetes.	LOW	CRITICAL
Renal dysfunction impact on benefits: ACE inhibitor vs. placebo									
3	randomized trial	serious limitations	serious inconsistency	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses in two trials. Composite endpoint not exactly the same in these two trials. The third trial evaluated total mortality instead of a composite endpoint.	ACE inhibitors may benefit those with renal dysfunction more than those without it.	LOW	CRITICAL
Hypertension impact on benefits: ACE inhibitor vs. placebo									
2	randomized trial	serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses in two trials. Composite endpoints not exactly the same in the two studies.	ACE inhibitors provide similar benefits to those with and without hypertension.	MODERATE	CRITICAL

Appendix C: Additional Evidence Tables and Analyses

Hypertension impact on benefits: ARB vs. placebo									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses in two trials. Composite endpoint not exactly the one selected in the CER.	ARBs provide similar benefits in those with and without hypertension.	LOW	CRITICAL
Hypertension impact on benefits: ACE inhibitor vs. ARB									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses in two trials. Composite endpoint not exactly the one selected in the CER.	ACE inhibitors may provide more benefits to those with systolic hypertension while ARBs may provide more benefits to those with normal systolic blood pressure.	LOW	CRITICAL
Hypertension impact on benefits: ACE inhibitor vs. ACE inhibitor + ARB									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses in two trials. Composite endpoint not exactly the one selected in the CER.	Combination therapy with an ACE inhibitor and ARB may provide more benefits in lower and higher systolic blood pressure ranges but patients with modestly elevated systolic blood pressure may benefit more from ACE inhibitor therapy alone.	LOW	CRITICAL
Baseline risk impact on benefits: ACE inhibitor vs. placebo									
1	Meta-analysis/ IPD meta-analysis	no limitations	single study	no serious indirectness	no serious imprecision	None	ACE inhibitors provide benefits in low, medium and high risk subjects. As baseline risk increases, the benefits derived from ACE inhibitor therapy might be accentuated.	LOW	CRITICAL
Baseline risk impact on benefits: ARB vs. placebo									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses in two trials. Composite endpoint not exactly the one selected in the CER.	ARBs may provide more benefits for those at lower baseline risk as compared to those at moderate to higher risk.	LOW	CRITICAL
Baseline risk impact on benefits: ACE inhibitors vs. ARBs									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses in two trials. Composite endpoint not exactly the one selected in the CER.	ACE inhibitor therapy might provide more benefits to those with moderate to high risk and ARBs may provide more benefits to those with lower baseline risk.	LOW	CRITICAL

Appendix C: Additional Evidence Tables and Analyses

Baseline risk impact on benefits: ACE inhibitor vs. ACE inhibitor + ARB									
1	randomized trial	serious limitations	single study	no serious indirectness	no serious imprecision	Only the composite endpoint included in subgroup analyses in two trials. Composite endpoint not exactly the one selected in the CER.	Combination therapy with an ACE inhibitor + ARB provides similar benefits as an ACE inhibitor alone regardless of baseline risk.	LOW	CRITICAL
Antiplatelet therapy impact on benefits: ACE inhibitor vs. placebo									
1	Meta-analysis/ IPD meta-analysis	no limitations	no serious inconsistency	no serious indirectness	no serious imprecision	None	ACE inhibitors may provide more benefits to those without concurrent antiplatelet therapy as compared to those with antiplatelet therapy. ACE inhibitors provide significant benefits versus placebo in both subgroups.	MODERATE	CRITICAL
History of revascularization impact on benefits: ACE inhibitors vs. placebo									
1	Meta-analysis/ IPD meta-analysis	no limitations	no serious inconsistency	no serious indirectness	no serious imprecision	None	ACE inhibitors may provide more benefits to those without a history of revascularization as compared to those with such a history. ACE inhibitors provide significant benefits versus placebo in both subgroups.	MODERATE	CRITICAL
Beta-blocker therapy impact on benefits: ACE inhibitor vs. placebo									
1	Meta-analysis/ IPD meta-analysis	No limitations	no serious inconsistency	no serious indirectness	no serious imprecision	None	ACE inhibitors provide similar benefits to those with and without beta-blocker therapy. ACE inhibitors provided significant benefits in those with and without beta-blockers.	MODERATE	CRITICAL
Lipid lowering therapy impact on benefits: ACE inhibitor vs. placebo									
1	Meta-analysis/ IPD meta-analysis	no limitations	no serious inconsistency	no serious indirectness	no serious imprecision	None	ACE inhibitors provide similar benefits to those with and lipid lowering therapy. ACE inhibitors provided significant benefits in those with and without beta-blockers.	MODERATE	CRITICAL
Vitamin E therapy impact on benefits: ACE inhibitor vs. placebo									
1	Randomized trial	no limitations	single study	no serious indirectness	serious imprecision	95% confidence intervals and p-values not provided for this analysis.	ACE inhibitors provide similar benefits to those with and without vitamin E therapy.	LOW	CRITICAL

Appendix D: Peer Reviewers

To Be Determined.

Appendix E: Abstraction Forms

Stable Ischemic Heart Disease Comparative Effectiveness Review

Study Characteristics

Ref ID:

First Author:	Citation:	
Language	Country(ies) Where Study Conducted:	Source of Study Funding:

Design Characteristics

Study Design:		Randomization Adequate?	Double-Blind?	Adequate?
☐ RCT - Parallel	☐ Obs - Registry	☐ Yes	☐ Yes	☐ Yes
☐ RCT - Crossover	☐ Obs - Cohort	☐ No	☐ No	☐ No
☐ Obs - Case Control	☐ Other:	☐ N/A	☐ N/A	☐ N/A
☐ Obs - Cross Sectional				

Allocation Concealment?	Adequate?	Intention-to-Treat?	If no, What was other method
☐ Yes	☐ Yes	☐ Yes	☐ Prospective Study Design
☐ No	☐ No	☐ No	☐ Propensity Score Matchin
☐ N/A	☐ N/A	☐ N/A	☐ Propensity Score Adjustec
			☐ Multivariate Analysis
			☐ Other:

Study Population

No. enrolled in Study:	No. Completed Study:	No. Withdrawals: Intervention 1: Reasons: Intervention 2: Reasons:

Run-in Period?	Describe Run-in Period:	% Removed During Run-in & Reasons:
☐ Yes		
☐ No		
☐ N/A		

Intervention 1 (drug, dose):	Intervention 2 (drug, dose):

Inclusion Criteria:

Exclusion Criteria:

Length of Study:	Duration of Patient Follow-up:

Appendix E: Abstraction Forms

Stable Ischemic Heart Disease Comparative Effectiveness Review

Baseline Characteristics

	Intervention 1	Intervention 2	Total
Males/Females:			
Average Age (years):			
White			
Hispanic			
African American			
Asian			
Other			
Average LVEF (%)			
Co-Morbidities			
Hx/o Angiographically Documented CAD			
Hx/o Myocardial Infarction			
Previous Revascularization			
CABG			
PTCA/PCI			
CABG or PTCA/PCI			
Hx/o Stable Angina			
Hx/o Unstable Angina			
Hx/o Stroke/TIA			
Hx/o Peripheral Vascular Disease			
Hx/o Diabetes			
Hx/o Renal Insufficiency			
Hx/o Hypertension			
Hx/o Left Ventricular Hypertrophy			
Hx/o Microalbuminuria			
Hx/o Smoking			

Appendix E: Abstraction Forms

Stable Ischemic Heart Disease Comparative Effectiveness Review

Baseline Characteristics

	Intervention 1	Intervention 2	Total
Systolic Blood Pressure (mmHg)			
Diastolic Blood Pressure (mmHg)			
Body Mass Index			
Total Cholesterol (mg/dl)			
LDL Cholesterol (mg/dL)			
HDL Cholesterol (mg/dL)			
Triglycerides (mg/dL)			
Glucose (mg/dl)			
Creatine (mg/dL)			
Potassium (mmol/L)			
Left Main			
Left Anterior Descending			
Left Circumflex			
Right Coronary Artery			
Baseline Medical Therapies			
Beta-Blockers			
Calcium Channel Blockers			
Aspirin			
Clopidogrel/Ticlopidine			
Antiplatelet			
Diuretics			
Nitrates			
Statin			
Lipid-Lowering			
Digitalis			

Appendix E: Abstraction Forms

Stable Ischemic Heart Disease Comparative Effectiveness Review

Efficacy Outcomes (Dichotomous)

	Intervention 1		Intervention 2	
	Number at risk	Number of events	Number at risk	Number of events
Primary Endpoint (list components)				
Total Mortality				
Cardiovascular Death				
Total Myocardial Infarction				
Fatal Myocardial Infarction				
Non-Fatal Myocardial Infarction				
Stroke				
Composite (CV death, non-fatal MI, stroke)				
Other Composite (list Components)				
Other Composite (list Components)				
Atrial Fibrillation				
Hospitalization				
No. of Ischemic Events				

Efficacy Outcomes (Continuous)

	Intervention 1		Intervention 2	
(n, mean+/-SD)	Baseline	Follow-up	Baseline	Follow-up
Exercise Time Before Ischemia				
Quality of Life (Scale used:)				

Appendix E: Abstraction Forms

Stable Ischemic Heart Disease Comparative Effectiveness Review

Safety Outcomes (Dichotomous)

	Intervention 1		Intervention 2	
	Number at risk	Number of events	Number at risk	Number of events
Hyperkalemia				
Cough				
Angioedema				
Syncope				
Withdrawals Due to Adverse Events				
Hypotension				
Rash				
Blood Dyscrasia's				